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The
Practical Medicine Series

COMPRISING EIGHT VOLUMES ON THE
YEAR'S PROGRESS IN MEDICINE AND SURGERY

Under the General Editorial Charge of
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Volume VI

Pharmacology and Therapeutics

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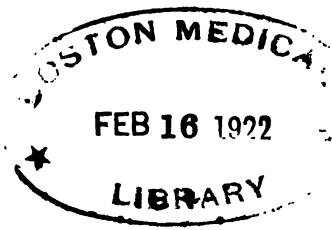
WITH THE COLLABORATION OF

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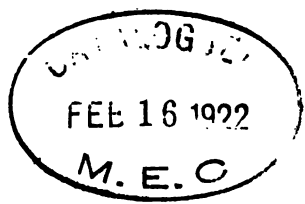


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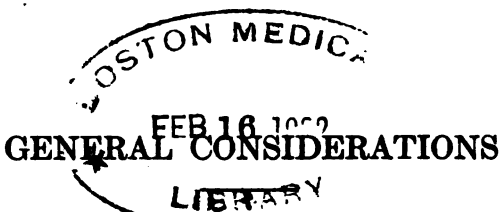
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PREFACE

It is probable that all the editors of the various subdivisions of the "Year Book" feel that theirs is the most important section of the "Practical Medicine Series." Naturally the editor of the part devoted to Pharmacology and Therapeutics shares the opinion of his distinguished colleagues. Like the others he has been embarrassed by the enormous volume of material poured in upon him when the cessation of the war reopened the floodgates of European literature. It required the exercise of much care to select some and reject the rest of it. As a general principle, work of no practical therapeutic value has not been reviewed. Demonstrations of the worthlessness of certain new and little used remedies, important as these studies are to the pioneer in therapy, have generally been rejected owing to lack of space. Wherever the editor entertained grave doubts about the soundness of an author's conclusions, the article has been withheld instead of indulging in derogatory editorial comments, as might have been his privilege. Errors in selection have no doubt been made. For these the readers' indulgence is requested.

BERNARD FANTUS.



U. S. P. and N. F. Revision. Not many physicians realize the amount of work involved in the revision of the U. S. P. and the N. F., as it is carried on so quietly and unobtrusively, even though actively, that some might not even be cognizant of the fact that such revision is now going on.

All over the country, research work is being done, the results of which may influence the revision.

The Official Elixirs. As the result of a study of elixirs by Fantus and Snow,¹ the suggestion is presented that the aromatic elixir of the U. S. P. be made "iso-alcoholic," that is, of an alcoholic strength just sufficient to dissolve the medicament for which the elixir is to serve as a vehicle. The aromatic elixir of the present U. S. P. contains approximately 25 per cent. alcohol, which is sometimes too much and sometimes not enough. Thus, if this elixir is to serve as vehicle for sodium bromide, potassium acetate, or sodium salicylate, no such amount as 25 per cent. alcohol is required or desirable, as alcohol accentuates taste sensation, hence the unpleasantness of the medication. If, on the other hand, it is to be used as diluent for fluidextract of cannabis indica or fluidextract of buchu, it is decidedly deficient in alcohol; and in both cases turbid unsightly mixtures result. Indeed, whenever there is a marked discrepancy between the alcohol strength of elixir and medicating preparation, as when tincture of digitalis, or of aconite, of veratrum, of nux vomica, of colchicum seed, or of lobelia is added to aromatic elixir, precipitates occur, which in some cases are liable to be toxic and dangerous. To enable the pharmacist to dispense iso-alcoholic elixirs, the pharmacopeia would have to recognize two basic

(1) Jour. Amer. Pharm. Ass'n., September, 1920.

aromatic elixirs: first, an aqueous elixir containing only 5 per cent. alcohol; and, secondly, an alcoholic elixir containing approximately 95 per cent. alcohol. These two would have to be mixable with each other in all required proportions. Formulas for these are given in the article. If iso-alcoholic elixir were introduced into the pharmacopeia and it were understood that the pharmacist would take care of the proper alcoholic strength of this vehicle, the physician—who can hardly keep in mind the alcoholic strength of all the menstrua used in the extraction of drugs—would not have to worry about incompatibility or alcohol solubility. The pharmacist, on the other hand, could easily, by means of his reference books, adjust to a nicety the alcohol percentage required. Incidentally it might be noted that the alcoholic elixir proposed, as it contains saccharin instead of sugar, might be used as a pleasant vehicle for medicaments intended for the diabetic.

The National Formulary contains a number of elegant vehicle elixirs that physicians are not sufficiently acquainted with. *The aqueous elixir of glycyrrhiza* of the N. F., which contains only about 5 per cent. of alcohol and the aroma of the compound spirit of cardamon and of orange flower water, is recommended by Fantus and Snow as a delightful vehicle, the best in their experiments, for salines such as sodium bromide, potassium acetate, sodium salicylate.

The compound elixir of almond of the N. F. is also a low alcohol elixir as it contains only 5 per cent. alcohol, the *compound elixir of cardamon* and the *compound elixir of vanillin* are other examples of elegant vehicles.

One or the other of these vehicle elixirs might with advantage be introduced into the pharmacopeia, which would give it greater prominence and more use, as physicians, unfortunately, are even less acquainted with the N. F. than they are with the U. S. P. In the art of prescribing, a good knowledge of vehicles is of the same importance as a liberal variety of spices and condiments in the art of cooking. Just as "we can live without art, but not so well," so we can get along without artistic perfection of our medicaments, but by no means so well.

The use as vehicle of the elixir of pepsin and of the

compound elixir of pepsin and rennin has no scientific foundation, inasmuch as the digestive ferments are practically never absent from the stomach in cases of dyspepsia, and it is difficult to see how the presence of these ferments in a medicament could make it more acceptable to a stomach that has an abundance of ferments, especially as it is well known that a slight increase in the amount of ferment does not measurably increase digestive activity. The practice is, no doubt, a survival of the day—not so long past—when the digestive ferments were hailed, even in scientific circles, as a panacea for digestive disorders. Commercial interests have been and are still at work to keep the fallacy alive.

While the National Formulary, as has just been noted, contains quite a variety of elegant vehicle elixirs, it is a curious fact that the Formulary does not itself make use of this variety, but directs nearly all the medicated elixirs to be made by the mere addition of the medicament to the aromatic elixir. This would be excusable if aromatic elixir were the ideal all-round vehicle; but this is by no means the case. Each of the N. F. elixirs ought to represent a masterpiece of the pharmacist's art; and experiments have shown that each elixir, or at least each class of elixirs, requires individual study. Suggestions are made, in the article cited, for the improvement of some of the N. F. elixirs. It would be of advantage to the popularity of the N. F. elixirs among physicians, if each teaspoonful of the medicated elixirs contained a medicinal dose, as has been suggested by H. C. Wood, and if each of the medicated elixirs were as pleasant a liquid administration form of the respective medicament as the combined skill of American pharmacists could devise.

DOSAGE

Rule for Calculation of Dilutions. W. Fletcher² presents a mathematical trick for quick calculation on making higher from lower dilutions.

“The average civilized man knows how to prepare a 40 per cent. solution from one of 80 per cent. by taking

(2) *Lancet*, Feb. 19, 1921.

one part of the latter and making it up to two parts by adding an equal quantity of diluent. This is the same thing as taking 40 parts and adding sufficient diluent to make 80. What is not generally realized is that all other dilutions can be prepared on the same principle; for example, a 30 per cent. solution can be made from one of 50 per cent. strength, by taking 30 parts of the latter and making it up to 50; or a 40.25 per cent. solution can be prepared from one of 79.5 per cent. by taking 40.25 c.c. of the latter and adding sufficient diluent to make 79.5 c.c. That is to say, an X per cent. solution can be prepared from a Y per cent. solution by taking X c.c. of the latter and diluting it sufficiently to make Y c.c."

"The preparation of the other fractional dilutions is equally simple. As every one knows, a 1 in 10 solution (written $\frac{1}{10}$) can be made from a 1 in 5 ($\frac{1}{5}$) solution by taking 5 parts of the latter, and diluting it up to 10 parts; but it is not generally known that all dilutions can be prepared in the same way; that, for instance, a $\frac{1}{97}$ dilution can be made from a $\frac{1}{8}$ dilution by taking 8 parts of the latter and making it up to 97. In short, a $\frac{1}{X}$ solution can be prepared from a $\frac{1}{Y}$ solution by taking Y c.c. of the latter and adding sufficient diluent to produce X c.c." By this method the medical man can not only calculate quickly but do it "in his head."

In this connection, B. Blacklock³ calls attention to the simple formula of Stephens and Christophers, which shows the amount of diluting fluid necessary to add to 1 volume of fluid of percentage X in order to reduce that volume to the desired percentage Y. The formula is $\frac{X}{Y} - 1$ where X represents the original percentage and Y the desired percentage. Thus, to dilute a solution from 20 per cent. to 5 per cent., add to each volume of solution $\frac{20}{5} - 1 = 3$ of the diluting fluid. The following formula can be used where it is necessary to prepare specified volumes of lower percentage or higher dilution from higher percentages and lower dilutions respectively.

Percentage Dilution: To prepare a specified volume

(3) *Lancet*, Feb. 18, 1921.

Z of a Y per cent. solution from an X per cent. solution, take of the latter $\frac{Y}{Z \times X}$ volume and make up to Z volume with diluting fluid.

Example: To obtain 12 c.c. of a 24 per cent. solution from an 80 per cent. solution, take of the latter $\frac{12 \times 24}{80} = 3.6$ c.c. and make up to 12 c.c. with diluting fluid.

Fractional Dilution: To prepare a specified volume Z of a $\frac{1}{Y}$ dilution from a $\frac{1}{X}$ dilution, take of the latter $\frac{Z \times X}{Y}$ volume and make up to Z volume with diluting fluid.

Example: To obtain 60 minims of a $\frac{1}{100}$ dilution from a $\frac{1}{10}$ dilution, take of the latter $\frac{60 \times 10}{100} = 6$ minims, and make up to 60 minims with diluting fluid.

Correct Determination of Ascending and Descending Dosage. Ernst Föld⁴ emphasizes the unsuitableness of the ordinary sequence of figures for the determination of gradual and progressively increasing dosage. Thus, for instance, if we were to increase dosage from 1 to 2, then to 3 etc., the proportion of increase will be much greater at first when we double the dose than, let us say, when we increase the dose from 9 to 10, in which case, the increase would be approximately 10 per cent. To increase dosage by equal gradations, which is so important in immunization therapy, as in vaccine and tuberculin treatment, the following row of figures would have to be employed.

1.0
1.29
1.67
2.15
2.78
3.59
4.64
6.00
7.74
10.00

(4) Therap. Halbmonatsh, May 15, 1921.

It will readily be seen that, by moving the decimal point, the series can be prolonged indefinitely.

However, these quantities are not convenient for weighing or measuring. Hence, Fuld suggests the following procedure. Make progressive dilutions 1 to 8 rather than 1 to 10, as follows:

| | |
|---------------|--------------|
| 1st dilution | 1:8 |
| 2nd dilution | 1:64 |
| 3rd dilution | 1:512 |
| 4th dilution | 1:4096 |
| 5th dilution | 1:32768 |
| 6th dilution | 1:262144 |
| 7th dilution | 1:2097152 |
| 8th dilution | 1:16777216 |
| <hr/> | |
| 9th dilution | 1:134217728 |
| 10th dilution | 1:1073741824 |

From any one of these solutions two further dilutions are prepared, the one seven times (designated for brevity's sake, solution "S") and the other five times designated solution "F." Now commence by using one part of solution "S," then one part of solution "F," next as follows: 2 "S," 2 "F," 4 "S," 4 "F," and next use one part of "S" of the next higher eight times stronger solution.

If, for instance, we desire to apply this method to Fowler's solution, we would first dilute the official solution 1:8 and then prepare two dilutions, one of these by mixing one part of Fowler's solution with six parts of water, and the other by mixing one part of Fowler's solution with four parts of water. If one desires to have the patient obtain these from the drugstore, the following prescriptions would be written:

R
 Solution of potassium arsenite..... 5.0
 Distilled water, to make..... 200.0

M. Label. Solution "F."

R
 Solution of potassium arsenite..... 2.0
 Distilled water to make..... 112.0

M. Label. Solution "S."

Directions: Teaspoonful "S" (containing 2 drops of Fowler's solution) three times daily; next teaspoonful "F," then two teaspoonfuls "S," then two teaspoonfuls "F," finally a table-spoonful "S" and a tablespoon "F."

For descending dosage, Föld recommends prescribing a bottle full of medicine which is kept constantly full by replacing the quantity taken out by equal the amount of water, as is also described by John Rice Miner⁵ who calls attention to the very gradual decrease of the dosage of morphine administered in the treatment of morphinism by the simple procedure of filling a bottle with distilled water to which is added a certain quantity of morphine. Enough of this mixture is administered as a first dose so that the morphine content will approximate the amount to which the patient has been accus-

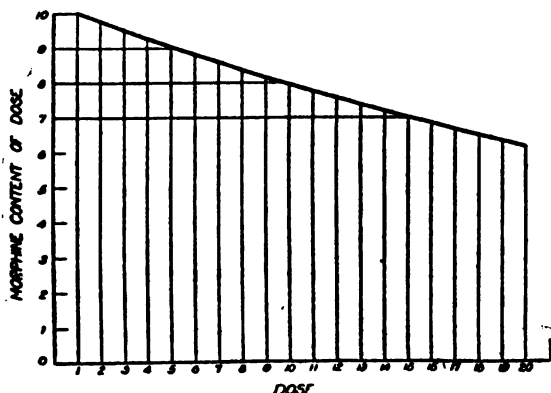


Fig. 1. Morphine content of successive doses. The curve appears at first glance to be a straight line but it is really slightly convex to the base.

tomed. After removal of the dose it is replaced by an equal volume of distilled water. The second and subsequent doses are of the same volume as the first, but, as each time enough water is added to maintain the original volume of the mixture, the morphine content of the doses thus administered diminishes steadily.

That the reduction is very gradual will be seen from Figure 1. At the tenth dose, the morphine content is diminished by only one-fifth, and even at the twentieth dose by less than two-fifths. The decrease in dosage is much slower than might be supposed on first thought. A stage where the dosage of drug would be $\frac{1}{10}$ of the

(5) Bull. Johns Hopkins Hosp., June, 1921.

original dose would occur only at the ninety-second dose in the series. Incidentally it should be noted that the morphine would never entirely disappear from the bottle.

The Principles Underlying Repetition of Medication for Curing Infections. Ronald Ross⁶ calls attention to the fact that, inasmuch as we can not extirpate the invaders after a single dose, we must repeat dosage much oftener than we had supposed to produce complete cure. A heroic dose of quinine put straight into the blood is cast out by it almost at once, while a much more moderate dose is likely to remain there longer and to do its work. Probably this accounts for the little difference observed between the effects of small and of large doses, of say, 10 grains a day and 100 grains a day. Hence, we may well suspect that there has been some fallacy in the arguments which led to the adoption of the larger dosage. We must disabuse ourselves of the notion that the parasites in a host are like fish in a bowl, which can be destroyed all together by mixing a single dose of poison in the water. They must be much more like the enemy on a battlefield, many of whom in their trenches and dug-outs will escape the most violent barrage, and there must be many recesses and backwaters of the circulation, which no medication bearable by the host can reach. If we lift the barrage for a long enough interval the enemy will immediately begin to bring up reinforcements in the form of spores and make good what reduction we had previously succeeded in effecting.

The author shows by calculation that if, for example, 30 grains of quinine reduce the number of plasmodia to one-half; then, in order to reduce 1,000 million of them to 1 we must probably repeat this dose, not twice nor thrice, but thirty times; and even after this we must continue to repeat it, say, four or more times in order to make nearly sure of destroying the last remaining plasmodium and its spores. But, if the reduction rate is only 0.8, which seems more nearly correct for quinine in malaria, as shown by studies of Thomson and the author, then, ninety-three doses should reduce the parasite population to 1. But this will not extirpate the infection entirely, for we must still destroy the *last*

(6) Brit. Med. Jour., July 2, 1921.

plasmodium. The chances against doing so by a single additional dose will be 5 to 1, for a reduction rate of 0.8 ($=\frac{4}{5}$), because in such case only 1 out of 5 parasites is destroyed by the single dose. Hence, this means another ten or eleven doses; but even this by no means quite exhausts the chances of survival which the last of the invaders may possess.

If the treatment be interrupted long enough to allow large numbers of organisms to proliferate in the interval, then the final result will receive a set-back. Calculating on the basis of the incubation period we may judge that *P. vivax* multiplies roughly at the rate of ten to one every two days, and *P. falciparum* still more quickly. Hence, perhaps we may infer that any intermission of continuous treatment for one or two days may allow the invaders to multiply ten times in the interval, thus undoing all the good work effected by the whole number of doses given. The reason why most returned patients continue to relapse is that they stop their quinine (often on medical advice) a few days or a few weeks after an attack of fever. Suppose that during this period they have reduced the invaders to 1,000, then ten or twelve days afterward the numbers will again return to the fever point, the patient will take more quinine, will stop it again too soon, and so on indefinitely, allowing relapse to follow relapse for months or years. The clinician must warn the patient strongly that the remission of quinine for one or two days will cost him all the fruits of from seven to ten days' previous treatment. Anything under 60 grains a week appears to be almost useless in the large majority of cases; and anything over 15 grains daily seems to be required only when there is fever, and say for a week or fortnight afterward, followed, of course, by the 10 or 15 grains daily for months. From clinical results extending over forty years, Ross thinks that a 10-grain daily dosage carried out rigorously for three months (84 days) is sufficient in the large majority of cases. In early infections perhaps four months would be safer. In clinic, Thomson and Ross have treated 24,000 cases of real or alleged malarial infection on this principle, and have found that the large majority who take their quinine properly seem to be cured; but those

who do not take their medicine, or who are given doses below 10 grains daily, or for whom "tonics" etc., are substituted for quinine, generally relapse. Though some may be cured of malaria under three months' continuous quinine course, which probably depends upon two factors—the patient's own parasitocidal bodies and the receptivity of his blood for the drug—we never know when this is going to happen; and it is therefore seldom safe to order less than the three months' course from the date of the last relapse.

At his clinic Ross has also had very encouraging results as regards intestinal amebiasis from a form of continuous medication with ipecacuanha, giving from 3 to 10 grains of powdered ipecacuanha in pill, without any adjuvant, on an empty stomach at bedtime every night for months without fail.

METHODS OF ADMINISTRATION

Proctoclysis by the Flush Method. B. V. Clanahan⁷ describes a method for the rectal administration of fluid that is practically fool-proof, gives greater comfort to the patient, and allows passage of feces, gas and returned solution *through* the rectal tube instead of around it. The apparatus consists merely of an irrigating can and a rectal tube with the end cut off. The can rests on a small table at the bedside at about the level of the patient's rectum, and care should be taken at all times that the top of the level of the fluid in the can be not more than 4 inches above the level of the rectum of the patient. The rectal tube extends from the can, under the bed clothes into the rectum of the patient. No regulation of flow is needed, and thus a constant to and fro communication is maintained between the large bowel and the container of fluid at the bedside. The tension which is caused by the head of pressure in the tube of the average drip method apparatus is a detriment rather than an advantage to absorption. It is much easier to keep the fluid in the flush method apparatus at an even temperature than in the drip method apparatus.

(7) Jour. Amer. Med. Ass'n., Jan. 15, 1921.

Continuous Subcutaneous Infusion. Strübing⁸ recommends continuous introduction of physiologic salt solution preferably with the addition of 0.006 to 0.010 gm. of epinephrine, by means of an apparatus such as is used in the drop enema. The needle is fastened to the skin by means of adhesive plaster. The rate of dropping is so regulated that no more is injected than can be absorbed, which usually amounts to approximately two drops a minute. Such injections have raised subnormal blood-pressure and improved the patient's general condition in the cardiovascular depression of infectious diseases. This procedure has also been found more efficient in severe bronchial asthma than the usual administration of epinephrine.

[This subject was discussed in the Practical Medicine Series, 1920, Vol. VI, p. 8.—Ed.]

Venipuncture of the Superior Longitudinal Sinus in the New-Born. J. Whitlock Gordon⁹ has performed 231 superior longitudinal sinus venipunctures without untoward results. This method is recommended by him as the best of any so far reported for obtaining blood or giving intravenous medication to infants. The head was not shaved and iodine was not used. The area over the anterior fontanelle was washed with 70 per cent. alcohol. The posterior angle of the anterior fontanelle was selected as the most desired location, because here the sinus is about $\frac{3}{32}$ inch (2.4 mm.) in diameter. The needles which work best are short beveled, at an angle of about 45 degrees, with a large bore No. 18. An assistant firmly holds the baby's head, when the operator inserts the needle at a slight angle. About $\frac{1}{4}$ inch (6.35 mm.) is the usual distance to the sinus from the skin. The blood is usually withdrawn easily. In the 231 operations he has failed to obtain blood only three times.

Gordon has successfully given from 60 to 180 c.c. of fluid intravenously by this route. Occasionally slight pressure must be exerted over the puncture site for about ten or twelve minutes to stop hemorrhage.

(8) *Deutsch. med. Wochenschr.*, 1921, p. 469.

(9) *Jour. Amer. Med. Ass'n.*, Nov. 28, 1921.

Intraperitoneal Infusion. F. Loewenhardt⁹ finds that in adults intraperitoneal injection of from 1.5 to 2 liters of fluid (Ringer's or physiologic salt solution with or without addition of dextrose or medicaments) is of advantage by reason of its comparative painlessness and rapid absorption, especially in those cases in which intravenous injection is difficult, as in patients with poorly developed veins and in very restless individuals. The injection is made, after careful iodine disinfection of the skin, at the junction of the outer and middle third of a line connecting the umbilicus with the anterior superior iliac spine. It is best to employ for this purpose a fine, none too sharp needle with a short, rounded point. The moment the peritoneum is entered the fluid is permitted to run in under moderate pressure.

M. Weinberg¹⁰ suggests making a small cut through the skin by means of a scalpel and then forcing a completely dull needle in a rotary manner through the rest of the abdominal wall. He also recommends, as the best place for puncture, the junction of the outer and middle thirds of a line connecting the umbilicus with the anterior superior spine of the ilium.

[The subject of intraperitoneal injections in infants and children was discussed in the Practical Medicine Series, 1920, Vol. VI, p. 94.—Ed.]

Intraperitoneal Administration of Dextrose. H. L. Moore¹ has obtained favorable results in marasmus by giving daily from 250 to 400 c.c. of 5 per cent. dextrose in physiologic salt solution. The treatment is continued until there has been a steady gain in weight, to be resumed if necessitated by loss of weight.

Intravenous Injection. C. C. Lund, A. Shaw and C. K. Drinker² studied the distribution of manganese dioxide particles, below 1 micron in size, one hour following intravenous injection in cats, dogs, rabbits, guinea-pigs, rats, chickens, and turtles. This distribution is remarkably constant for all the animals tested, except the cat, in which the injected material is practically equally divided between the lungs and the liver. In the other

(9) Zentralbl. f. inn. Med., 1921, p. 194.

(10) Münch. med. Wochenschr., 1920, p. 1264.

(1) South. Med. Jour., May, 1921.

(2) Jour. Exper. Med., February, 1921.

animals, the liver performs the main share of the work; and in the cat it has been shown that the liver after twelve hours accumulates the manganese which was formerly deposited in the lungs.

The results are in harmony with experiments in which bacterial suspensions are employed for injection and confirm the suggestion made that in the first handling of foreign particulate material the animal behaves similarly whether protein or inorganic injections are used.

H. A. Rosenbaum³ suggests the use of an ordinary scarf-pin clasp, to keep the needle from passing through the vein it has successfully entered, slipped on the needle with the adjusting globoid portion of the clasp opposite the point of the needle. When entering the vein the clasp is well up on the needle, and as soon as the vein has been entered an assistant slips the clasp down to



Fig. 2. Scarf-pin clasp on needle in position before vein is entered.

the skin. These easily adjustable clasps may be found at any jeweler's or haberdasher's.

For longitudinal sinus work in infants, needles are now used which have a stationary bulb the proper distance from the point as required for this operation.

Intracardiac Injection. This method, to which attention was directed in the 1920 "Year Book" (Vol. VI, p. 11), has been made use of during the past year with increasing frequency and success. E. Vogt⁴ speaks of fifteen successful cases in some of which there had been respiratory standstill for five minutes and, in a case reported by Vogt, even fifteen minutes. The author considers intracardiac injection the simplest and most certain method to cause the motor of the circulatory apparatus to resume motion and to effect resuscitation. The fact that the heart is "*primum movens sed ultimum moriens*" (the first to move, the last to die) gives the procedure its justification. It has been shown experi-

(3) Jour. Amer. Med. Ass'n., July 2, 1921.

(4) Münch. med. Wochenschr., June 17, 1921.

mentally that the limit of recovery lies not so much with the heart as with the much more sensitive brain, which does not tolerate circulatory standstill for more than a few minutes. Hence, the important thing is to act promptly and resolutely. The chief remedy for intracardiac injection is epinephrine, the effect of which upon the heart is wonderful. This drug was used in nine of the fifteen successful cases. Quite as important as its effect is its harmlessness, even when injected into the heart muscle itself. This can not be said of other circulatory stimulants such as camphor, caffeine, digitalis, or strophanthin, all of which are liable to damage the muscle into which they are injected. A dose of 1 c.c. of the 1:1000 solution must be looked upon as a maximum. Next in value is the solution of hypophysis, which though feebler in action is possibly safer in cases of arteriosclerosis, myocardial degeneration, the heart hypersensitiveness of hyperthyroidism, and in nephroses.

The following technique is advised: Injection to be made into the fourth or fifth intercostal space just to the left of the sternum. After iodine disinfection, the needle is inserted at the upper margin of the fifth or sixth rib starting down along the edge of the sternum until its posterior surface is reached. Now its point is turned toward the midline as it is pushed through the heart until the resistance of the heart muscle ceases suddenly. Entrance into the heart is indicated by the appearance of blood in the syringe. The imparting to the needle of even feeble motion by the heart is a favorable sign. To avoid pneumothorax and pneumopericardium, the needle is to be inserted and withdrawn while attached to the syringe. When, as is nearly always the case, this injection is done during artificial respiration, it should be performed in the expiratory phase.

Vogt distinguishes between three forms of intracardiac injection. The intrapericardiac, the intramyocardiac, and the intraventricular. It is the third form of injection which is the most effective and should be aimed at.

Intratracheal Administration. F. Guyot⁵ advises supraglottic injection because simpler and as efficient as

(5) Bull. d'oto-rhinol., 1920, p. 233; abstr. in Therap. Halbmonatsh., May 1, 1921.

the subglottic method, which can only be practiced by the specialist.

The tongue having been pulled forward, the tip of the syringe is introduced without touching the root of the tongue; and about 1 cm. in front of the posterior pharyngeal wall, it is depressed by raising the hand, so that it is held just above the opening of the larynx. While the patient is ordered to inhale deeply, the injection is quickly accomplished. Beginners will do better to inject doses of 5 c.c. in two or three portions. For injection gomenal (5 per cent.) guaiacol (1 to 5 per cent.) or menthol (1 per cent.) are used in olive oil, which has been washed with alcohol.

Favorable results have been obtained with this method in tracheitis, bronchitis, and bronchopneumonia, tracheal ozena, severe asthma, and most especially in laryngeal and pulmonary tuberculosis, in which daily injections of from 5 to 10 c.c. of 5 per cent. gomenal oil for three or four weeks have removed secondary infection, cough, and fever.

Favorable results have also been obtained in twelve cases of pulmonary gangrene with from ten to twenty-four injections administered by the supraglottic method by J. Guisez.⁶ He employs at least 20 c.c. of fluid; less, he says, does not reach the lung. The patient's trunk should be bent to one side, so that the fluid drops directly into the diseased bronchus. Coughing must be prevented by anesthesia of the larynx and trachea.

ETIOTROPIC THERAPY

The Use and Abuse of Antiseptics. H. R. Owen⁷ believes much harm is done by indiscriminate disinfection of wounds. He has seen more evil than good result from iodine used as a first-aid expedient. This is not because of its use but because of its abuse. The difference between the use of iodine as a disinfectant of a wound, as a disinfectant of the skin and as a counterirritant, does not seem to be sufficiently emphasized by the surgeon. Certainly this distinction is understood imperfectly by

(6) Presse méd., Feb. 26, 1921.

(7) New York Med. Jour., June 15, 1921.

the first-aid worker. The same strength is often used erroneously for every purpose.

The application of iodine followed by a hot bichloride of mercury compress always causes severe irritation of the wound with actual vesication of the surrounding skin. A basin of bichloride of mercury should not be permitted in the same room in which iodine is being used.

Owen asks: "Does bichloride of mercury ever do any good whatsoever in surgery?" He believes that if bichloride of mercury should pass into the state of surgical desuetude the sole mourners would be undertakers.

Peroxide of hydrogen is a cleansing agent, not a germicide. It may be used to clean a dirty wound or to assist in the removal of small particles of dirt or other foreign bodies. It should not be used in a sterile wound. If used in the treatment of boils and carbuncles or abscesses, the liberation of oxygen in the presence of pus will tear tissues, break down normal barriers, and spread infection.

By properly cleansing a wound is not meant washing the wound with peroxide or bichloride, but removing all foreign bodies and devitalized tissues, shaving the hair surrounding the wound, and washing the wound and surrounding skin with neutral soap and water, followed by ether. Ether is a most useful agent. In first-aid work, Owen uses more ether than iodine. The wound and surrounding skin are washed with ether, and a sterile dressing is applied. Very often a wound can not be properly cleansed without an anesthetic. Many wounds will heal readily without any treatment other than daily cleansing of the wound and surrounding skin. Too much stress can not be laid upon the necessity of the daily removal of all crusts from the edges of the wound. Under these crusts are harbored the bacteria which retard granulations. Those who take routine cultures of wounds know that often after the surface of a wound is sterile a positive culture can still be obtained by passing the platinum loop under these crusts. A large infected wound should be treated with the instillation of Dakin fluid by the Carrel technique; *débridement* should be practiced when indicated. An infected wound

of smaller size can be treated with chlorinated oil. Dichloramine-T must be watched closely each day, as it becomes rancid. A rancid oil will often cause irritation. When a wound is sterile it will heal without the further use of antiseptic provided there is no secondary contamination. Some sterile wounds can be closed with secondary suture. Upon a sterile granulating wound, not suitable for secondary sutures, paraffin mesh and a sterile gauze dressing or salt solution should be applied. The paraffin mesh prevents the gauze from sticking to the granulations, permits sufficient drainage of secretions and, by making pressure, tends to prevent flabby or exuberant granulations.

Unhealthy granulations are frequently due to infection or the use of too strong an antiseptic. In many cases of delayed healing the patients will be found to be suffering from anemia, Bright's disease, syphilis, or diabetes.

A punctured wound should be opened by crucial incision, searched with dressing forceps for foreign bodies, washed with ether, and drained with rubber tissue. Phenol had better not be used as it causes necrosis of tissue and suppuration. Stick silver nitrate is in the same category.

Burns and scalds should be treated antiseptically, utilizing the same principles of surgery which apply to the treatment of wounds. Burns should not be treated with greases or pastes or with dirty preparations such as carron oil. A burn should be cleansed in the identical manner in which a wound is cleansed. The hairy portions of the skin surrounding a burn should be shaved. An anesthetic is often necessary to permit the proper cleansing of a burn. Sloughs should be loosened with an antiseptic compress, then cut away. A healthy granulating surface must be kept free from infection and pressure should be applied over the granulations. Paraffin gauze mesh or petrolatum gauze (which is more pliable) may be used for the purpose of protecting granulations. This gauze should be of wide mesh in order not to dam secretions and at the same time permit access of an antiseptic solution if necessary. The petrolatum gauze is sterilized before being used. An infected

burn can be treated by Dakin's solution if the patient does not find it too painful. At times this solution may be used with comfort; at other times it causes severe pain. Dakin oil may be used. This is not so painful as the solution. If this oil is to be used daily, the strength should be 0.5 per cent., or 1 per cent.

Colonic Antiseptic Treatment. Norman⁸ believes that in the search for foci of infection in chronic diseases not only the teeth, the sinuses, the antra, the tonsils, the gall-bladder, appendix, the prostate and the Fallopian tubes should be scrupulously inspected, but also the colon, which he considers the most important infection site. In the treatment of colonic infection, Norman first washes out the colon with antiseptic solution, and then attempts the implantation of bacteria antagonistic to the pathogens. He employs the following technique: A soft rubber tube from $\frac{3}{4}$ to $\frac{7}{8}$ of an inch in diameter and from 33 to 44 inches long is used. Two percolating jars, one of three gallon and the other of one gallon capacity, are needed. They are suspended about two feet above the level of the anus. These jars are arranged so that either one may be cut off and both flow through a three-way valve which, in one position, allows of the flow of water from the jar into the patient's colon, and when in another position cuts off the flow of water from the jar and allows of the siphonage of the water from the patient to the waste jar. He begins with Dakin's solution prepared from hychlorite, and passes the tube as far as possible; then he siphons out all the solution possible, and instils a quart of hot 1:500 or 1:1000 potassium permanganate solution. While doing this, by tilting the table to about a twenty-degree angle, with the patient's head depressed, one may palpate and auscultate the fluid running through the transverse colon to the cecum. The patient is allowed to rise and expel the contents. Daily washings are given until the feces become a yellow color and the bacteriologic picture shows an improvement. When this occurs we may introduce into the colon fresh, live cultures of Bulgarian and acidophilus bacilli with a large quantity of sugar of milk, which is excellent food for their growth. These bacilli

(8) New York Med. Jour., April 6, 1921.

secrete lactic acid and thus create an environment unfavorable for the growth of pathogenic organisms. In addition to this, they are healing to the inflamed mucosa. The cultures are kept up until the patient has reacted favorably, when the *B. bulgaricus* is dropped from the culture, the *B. acidophilus* being planted until the stool examination assures the physician of the permanency of its growth.

IODINE

Iodine for Sterilizing Site of Hypodermic Puncture.

C. J. Marshall⁹ describes an iodine swab (Fig. 3) which fits nicely in the case alongside of the syringe. It is made of two empty hypodermic tablet tubes, a bit of small rubber catheter, $\frac{3}{4}$ inch long, of a size to slip inside the tube, 1 inch of very small glass tubing, and a

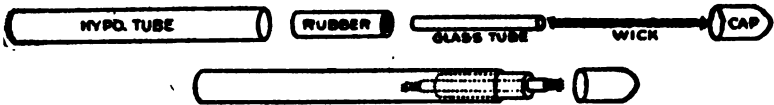


Fig. 3. Contrivance for sterilizing the site for a hypodermic puncture. It may be carried in the hypodermic case.

little thread for a wick. The thread is loosely twisted, about eight strands, and pulled inside the small glass tubing. This, in turn, is put in the section of rubber tubing. One of the tablet tubes is half filled with tincture of iodine, and the assembled glass, rubber and wick are slipped in the end of the iodine tube, making a tight fit. About $\frac{1}{8}$ inch of the wick is left protruding beyond the end of the glass tube; this becomes saturated with the iodine, and is used as a swab. A cap for the outfit is made by heating the other empty tube in the flame, about half an inch from the open end, melting and drawing it in two, thus closing the open section, and forming a tight cap which fits over the wick. The whole may now be carried with perfect safety in the hypodermic case.

The Use of Iodine to Break Up a "Cold." H. Koenigsfeld¹ speaks favorably of a recommendation by

(9) Jour. Amer. Med. Ass'n., April 9, 1921.
 (1) Therap. Halbmonats., May 1, 1921.

J. Finck (1920) of the use of iodine in the following manner:

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| Iodine | 0.10 |
| Potassium iodide | 1.00 |
| Distilled water | 10.00 |

Of this, adults receive from 8 to 10 drops in a quarter of a glass of water to be followed by one-half a glass of water. Children up to the age of 10 years are given 5 drops. The important thing is that the remedy be given promptly at the earliest possible moment; for instance as soon as sneezing begins. It is best kept on hand, as occasion for using it occurs evenings or even during the night. The author states that a single dose used promptly often succeeds in preventing the onset of coryza or angina. If it does not, it may be continued twice daily—two hours after breakfast, and before going to bed—for two or three days; then once a day. The patient should also avoid chilling and over-exertion. In case there are headache, pains and subfebrile temperature, Koenigsfeld advises giving with the first dose of iodine from 1.5 to 2 gm. of aspirin. Finck believes that this treatment might be of prophylactic importance in measles, scarlet fever, influenza and variola.

Iodine in the Cerebrospinal Fluid. E. D. Osborne² found minute amounts of iodine present in the cerebrospinal fluid of normal individuals; and increased amounts following the administration of iodides by mouth, by rectum and intravenously. The iodine content of the cerebrospinal fluid following administration of iodide by mouth or by rectum is small compared with that following the administration intravenously (from 100 to 200 c.c. of 10 per cent. solution). Certain observations made in the course of this study suggest the possibility that (a) neurosyphilitic tissue takes up more iodine than normal nervous tissue, and (b) the presence of a meningitis increases the permeability of the meninges to iodine compounds in the blood.

[These observations might furnish justification for the intravenous administration of iodides in certain con-

ditions of the nervous system that prove exceptionally intractable to peroral administration. Otherwise, owing to the readiness with which iodides are absorbed, there would be little gained by the intravenous route.—Ed.]

Unusual Susceptibility to Iodine. H. E. Happel³ reports the case of a patient in whom, in the course of a supravaginal hysterectomy, he used a cotton-tipped applicator, dipped in tincture of iodine to touch the cervical stump. Less than a drop was employed. Seventeen hours later, the patient began to complain of intense itching and burning of the skin, with a sensation of swelling of face and hands. When the patient saw wheals appear on her arms and hands, she exclaimed: "They used iodine on me." The nurse examined the abdomen and found that picric acid solution had been used in preparation of the skin, and so informed her; but she insisted that iodine had been used somewhere, stating that about nine years before she had had a similar experience after painting the back of her neck with iodine to relieve soreness of the muscles. The rash was a typical urticaria involving the face, scalp, upper extremities, trunk and, to a less degree, the lower limbs. The intramuscular injection of 10 minims of epinephrine hydrochloride (1:1,000 solution), gave almost instant relief, the rash disappearing as if by magic; but it reappeared in about four hours. A second hypodermic of epinephrine produced the same effect, though not so promptly. The attack lasted two days. The attack nine years before had lasted one month.

MERCURY

Absorption of Insoluble Mercury Preparations from Intramuscular Injection. H. N. Cole, S. A. Littman and T. Sollman⁴ have followed the absorption of injected mercurials by means of Roentgen shadows with the following results:

Mercuric salicylate: By gluteal muscles, mean, four days; extremes, four to ten days. By lumbar muscles,

(3) Jour. Amer. Med. Ass'n., April 23, 1921.

(4) Jour. Amer. Med. Ass'n., Dec. 4, 1920.

mean eight and one half days; extremes two to beyond twenty-four days.

Calomel: Mean, fifteen days; extremes, four to thirty-nine days.

Gray oil: Unabsorbed during entire period of observation, a mean of forty-three days; extremes of sixteen to 125 days.

These findings indicate that gray-oil injections are both inefficient and dangerous, and their use should be abandoned. Calomel injections are dangerous. Mercuric salicylate injections, especially into the gluteal muscles, give a satisfactory absorption and present relatively little danger.

Mercuric Chloride in Antivenereal Prophylaxis. J. Schumacher⁵ condemns Metchnikoff's calomel ointment on the basis of the proposition that solutions are more effective than ointments. A 0.1 per cent. solution of mercuric chloride may well be recommended as a prophylactic against both syphilis and gonorrhoea. This solution should be applied to the carefully cleansed penis and the urethral orifice with the little finger dipped in the solution, or by means of a cotton-wrapped applicator.

Dosage of Mercury in Treatment of Hereditary Syphilis. Philip C. Jeans⁶ describes the following method which has given satisfactory results after four years' use in cases of hereditary syphilis.

"The child attends the clinic once a week. At each visit, 0.03 c.c. of a 1 per cent. solution of mercuric chloride for each kilogram of body weight is injected intramuscularly and mercury with chalk is prescribed three times daily by mouth in doses ranging from 13 mg. for small infants to 100 or even 130 mg. for the largest children. A laxative effect is avoided by decreasing the dose when necessary.

"Every two months there is started a course of three intravenous injections of arsphenamine given at weekly intervals. The dosage is 0.01 gm. for each kilogram of body weight. Mercury administration is not interrupted for the arsphenamine course."

(5) Deutsch. med. Wochenschr., June 2, 1921.

(6) Jour. Amer. Med. Ass'n., Jan. 15, 1921.

A rest period of from four to eight weeks is given during the first year of treatment, provided the attendance has been sufficiently regular. Such routine is continued for at least one year in infants, and with older children for at least two years, regardless of what the Wassermann reaction shows. Treatment is continued in the same manner for as much longer than this as seems indicated by the clinical signs or the Wassermann reaction.

Mercurochrome as a Germicide. H. H. Young, E. C. White, and E. O. Swartz⁷ present the following conclusions:

Mercurochrome has proved to be a very valuable drug in acute gonorrhoea, but the intense stain is a drawback to its use as an injection by the patient. Solutions of from 0.25 to 0.5 per cent. are sufficiently concentrated to produce a satisfactory germicidal effect in the urethra, and are always non-irritating. Emphasis should be laid on the desirability of using fresh solutions as Swartz and Davis have shown that the solutions deteriorate on standing. Acriflavine is free from the objection of staining; and, though not so good a germicide, is often preferable in acute cases.

In chronic infections of the urethra, prostate and vesicles the great value of mercurochrome has been amply proved. It penetrates deeply and may be found in the prostatic secretion several days after posterior instillation.

The results obtained in many cases of chronic cystitis are remarkable, long-standing infections often clearing up in a few treatments. The preliminary irrigation of the bladder with sterile water or physiologic sodium chloride solution to cleanse the bladder is essential. The solutions of mercurochrome should then be injected into the bladder and retained as long as possible. This may be repeated as often as three times a day, depending on the tolerance of the patient. At least two treatments daily should be given, if possible. It is best to begin with a weak solution, 0.5 per cent., and increase the strength of the solution to 1 per cent. in a day or two, though in many cases two injections of 1 per cent. solution daily are well-borne. In some cases which fail to become

(7) Jour. Amer. Med. Ass'n., July 9, 1921.

sterile constant reinfection of the bladder is found to occur from kidneys or prostate.

Mercurochrome is less irritating and produces less reaction in the renal pelvis than silver-nitrate solutions, while possessing about equal germicidal powers; but in some cases both drugs should be used alternately, and sometimes silver is better.

In some cases of pyelitis, the infection comes from the teeth, tonsils, etc., and sterilization of the renal pelvis is impossible until the primary focus is cured.

Continued use has proved it to be a most satisfactory dressing for venereal ulcerations and buboes. Reports indicate that mercurochrome is very valuable in dressing open wounds and sinuses. A 1 per cent. mercurochrome solution may be injected gently into a fistula with impunity, daily.

The germicidal efficiency of the drug in other branches of medicine and surgery, has been proved, especially in the treatment of infections of the throat, nose, sinuses, ear and eye and teeth. It is reported to be most efficient in disinfecting the throats of diphtheria carriers.

Mercurochrome-220 Action on Gonococcus. E. O. Swartz, and D. M. Davis⁸ encouraged by the strikingly high germicidal power of this drug against *B. coli* and *Staphylococcus aureus*, undertook tests with the gonococcus. An important feature of this drug is that its maximum action occurs in a short time, as compared with certain other drugs, such as the flavines, to secure the maximum effect of which contact must be maintained over a much longer period. The results of the tests showed that a solution of 1:16,000 of mercurochrome—220 kills gonococci in twenty minutes. If this is divided by the dilution at which it may be used in the urethra, 1:50 (2 per cent.), it will be seen that this therapeutic strength is 320 times as strong as that necessary to kill. The gonococcus is comparatively easily killed by chemicals, as is shown by the fact that a solution of mercurochrome-220 which will kill *B. coli* in twenty minutes is about forty times as concentrated as that required to kill the gonococcus in the same period. The staphylo-

(8) Jour. Amer. Med. Ass'n., March 26, 1921. by Google

coccus required about four times the strength necessary for *B. coli*.

These figures correspond well with those obtained with potassium mercuric iodide. Old solutions were found much less efficient. Some change, the nature of which has not been determined, occurs in solutions of mercurochrome-220 on standing which diminishes greatly its germicidal value. Hence, solutions of mercurochrome-220 should be made freshly for clinical use. The instability of the solutions may explain many of the conflicting clinical results, and failures to obtain the expected effects.

ARSPHENAMINE

A Simple Method of Preparing Solutions of Neo-Arsphenamine. J. F. Schamberg⁹ advocates the follow-

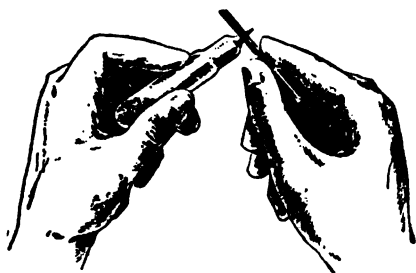


Fig. 4. Filing tip of ampule.

ing technique for the use of neo-arsphenamine: The ampule is shaken or knocked so that the powder flows easily and is not lumped. The tip of the ampule is filed off, as illustrated in Fig. 4. The opening should be large enough to permit the introduction of the needle to be used. With the ampule in almost horizontal position, 5 c.c. of sterile distilled water is introduced by means of the syringe (Fig. 5). The ampule is then agitated for from thirty seconds to a minute, when the powder should be in complete solution. To avoid spilling the solution, the finger, covered with a rubber glove or rubber finger

(9) Jour. Amer. Med. Ass'n., Jan. 15, 1921.

stall, should be held over the tip of the ampule. The solution is then drawn up into the syringe (Fig. 6) and is ready for injection. If one desires to use more water for the injection, 5 c.c. or as much as is desired can be placed in the syringe before sucking up the solution

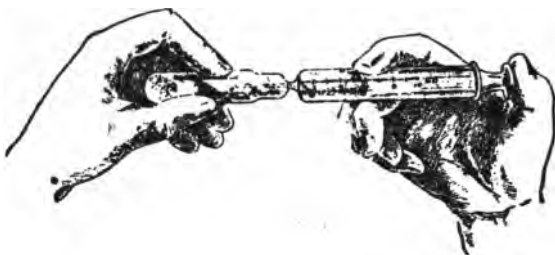


Fig. 5. Injecting distilled water into ampule.

from the ampule. At least from one to one and one-half minutes should be consumed in injecting 5 c.c. of solution. A solution should never be used unless it is brilliantly clear.

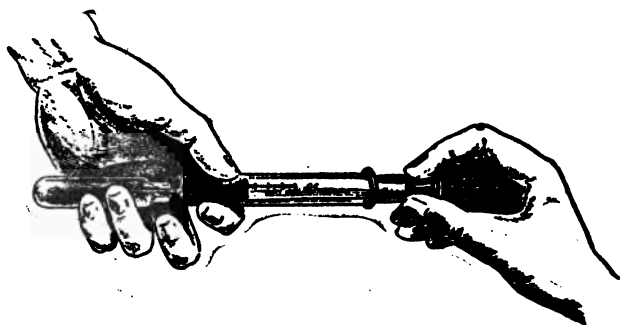


Fig. 6. Drawing solution of neo-arsphenamine into syringe.

Intravenous versus Intramuscular Administration of Arsphenamine. C. Voegtlin and H. Smith¹⁰ studied the relation between the minimum effective dose and the curative dose in rats infected with *Trypanosomum equiperdum*. The arsphenamine preparation used intraven-

(10) Jour. Pharm. and Exper. Therap., June, 1921.

ously was the disodium salt; for the intramuscular injection arsphenamine emulsified in olive oil was used. They found that the intramuscular and intravenous methods are equally effective in the treatment of rat trypanosomiasis, as judged both by the minimum effective dose and the percentage of survivals. It is largely on account of the irritant nature of arsphenamine and its substitutes that its intramuscular use was largely discontinued.

“Should it be possible, however, to reduce this local irritation, and there are reasons to believe this can be accomplished when neo-arsphenamine is used, the intramuscular injection of this drug in the treatment of syphilis should be given preference, on account of the simplicity of technique and the probability of reducing the number of acute toxic reactions.”

Rectal Injection of Massive Doses of Neo-Arsphenamine. H. G. Mehrtens¹ points out that rectal injections of arsphenamine have been used by a number of clinicians with varying results. The French were the first to use this method, and have been most enthusiastic in its advocacy. A number of American and British authorities, on the other hand, consider the rectal method ineffective. It is probable that the latter conclusion is correct with the dosage used. When, however, the dose is increased to 4 gm. of neo-arsphenamine, a dose which was safely given intrarectally in 125 cases, the arsenic is absorbed into the blood in large amounts, and larger quantities are eliminated in the urine than after ordinary intravenous injections of arsphenamine. The arsenic also persists longer in the blood in perceptible quantities after the rectal method with large doses than after ordinary intravenous methods (Fig. 7). About equal concentrations in the spinal fluid are obtained with either method.

The technique used for rectal injection was as follows: The patients were given a brisk purge on the day preceding the treatment. Two hours before the treatment they were given a colonic flush until the washings returned clear. Simultaneously with the injection, tincture of opium or paregoric was given by mouth, or, in some cases, morphine by hypodermic injection. The

(1) Jour. Amer. Med. Ass'n., Feb. 26, 1921.

arsphenamine or neo-arsphenamine was dissolved and neutralized just as for intravenous injection. The volume for each dose was 100 c.c. This was retained twenty-four hours, if possible.

The clinical results in the author's series are difficult to estimate. However, when the neo-arsphenamine injected rectally was used in full doses (*i. e.*, 4 gm.), improvement was at least as rapid as that formerly observed when the intravenous method was used, as judged by clinical manifestations, and more particularly by the

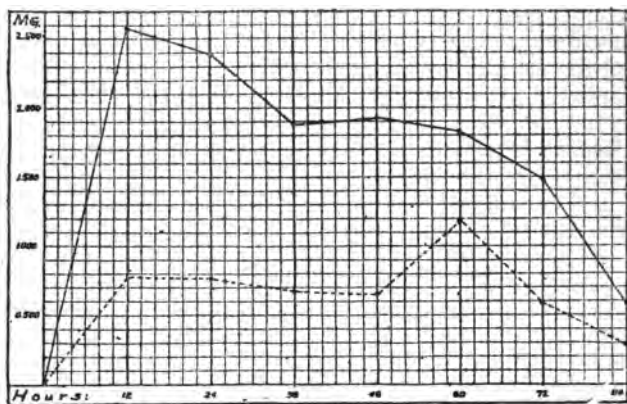


Fig. 7. Arsenic in urine; solid line, after rectal injection of 4 gm. of neo-arsphenamine; broken line, after intravenous injection of 0.6 gm. of arsphenamine.

clearing up of the Wassermann reaction and other reactions of the spinal fluid. In the beginning of this work, when arsphenamine was used, symptoms of rectal irritation appeared. For this reason, neo-arsphenamine was substituted. The dose of 4 gm. of neo-arsphenamine was never repeated oftener than once in seven days, and the intervals were usually from ten to fourteen days. The only signs of toxicity observed after these doses were the occasional attacks of vomiting, and puffiness under the eyes, which developed in two patients. Several patients received seven of these large doses in a series without showing ill effects.

All things being equal, the intravenous method of administering arsphenamine and neo-arsphenamine is still the method of choice in most cases. But, based on the foregoing observations, the author feels that the rectal administration of neo-arsphenamine has a place in therapy when massive doses are used, especially in the cases of children, those with difficult or impossible veins, and in individuals in whom, for any reason, intravenous injections are dangerous or undesirable.

The Effect of Shaking on Arsphenamine and Neo-arsphenamine. George B. Roth² found by experiments on rats that shaking alkalized aqueous solutions of arsphenamine or aqueous solutions of neo-arsphenamine in the presence of air renders them highly toxic. This increase in toxicity is presumably due to the oxidation of these compounds to p-oxyphenaylarsenoxide, commonly called "arsenoxide." Shaking a solution of neo-arsphenamine in the absence of air does not increase the toxicity of such a solution.

Arsphenamine Toxicity. This, according to Reid Hunt,³ is due to several factors, some of which he analyzes. Thus, he found the symptoms in rats caused by "arsenoxide" so characteristic that its presence in arsphenamine in a percentage too small to increase greatly the toxicity can readily be detected by the symptoms. Confirmatory evidence of the presence of "oxide" (or of some oxidation product of arsphenamine) in a toxic preparation of arsphenamine can be obtained by treating the solution with sodium hydrosulphite. This leads to an immediate diminution of the toxicity, if the latter is due to the presence of the "oxide." No toxic commercial preparations of arsphenamine have been encountered, the toxicity of which could be attributed to the presence of the "oxide." Some preparations of arsphenamine are very toxic when the solutions are prepared at ordinary room temperature; the toxicity is greatly reduced by gently warming and in some cases by allowing the solutions to stand for a time at room temperature. Cold may preserve the toxicity for long periods. Hunt considers that the undue toxicity of such preparations is

(2) Public Health Reports, Sept. 17, 1920.
 (3) Jour. Amer. Med. Ass'n., March 26, 1921.

probably due to the physical state of the solution, and that this undergoes a rapid change when the solution is warmed.

Toxic preparations of arsphenamine are sometimes encountered, the toxicity of which is due to factors other than the foregoing; the toxicity is not diminished by the action of sodium hydrosulphite or by warming; it is not due to inorganic arsenic and certain other compounds which have been suggested.

The Toxicity and Trypanocidal Activity of Sodium Arsphenamine. J. F. Schamberg, J. A. Kolmer, and G. W. Raiziss⁴ report the results of their studies of sodium arsphenamine compared with arsphenamine and neo-arsphenamine. They find the highest tolerated dose of sodium arsphenamine for white rats by intravenous injection to be from 212 to 215 mg. per kg. of weight. The average tolerated dose of arsphenamine was 105 mg., and of neo-arsphenamine, 200 mg. per kg. The smallest trypanocidal doses of sodium arsphenamine varied from 16 to 24 mg. per kg. of weight; the smallest trypanocidal dose of arsphenamine was 5 mg., and of neo-arsphenamine, 9 mg. per kg. The therapeutic dose of sodium arsphenamine was from eight to thirteen times less than the highest tolerated dose, which expresses the therapeutic index of this compound. The therapeutic dose of arsphenamine was twenty-one times less than the tolerated dose, and the therapeutic dose of neo-arsphenamine was twenty-two times less. Therefore, while sodium arsphenamine possesses the low toxicity of neo-arsphenamine, it is much inferior to both arsphenamine and neo-arsphenamine in trypanocidal or curative ability.

Absence of Effect of Arsphenamine on the Kidneys. B. Anderson⁵ failed to find any conclusive evidence of injury to the kidneys, after kidney functional tests on thirty-nine patients, each of whom had received from twenty to thirty doses of 0.46 gm. of arsphenamine.

Atropine and Epinephrine Useless Against Reactions Following Arsphenamine. A. A. Strickler⁶ concludes as a result of investigation that injections of either atro-

(4) Jour. Amer. Med. Ass'n., June 25, 1921.

(5) Amer. Jour. Med. Sci., July, 1921.

(6) New York Med. Jour., Oct. 2, 1920.

pine sulphate in the dose of gr. $\frac{1}{75}$, or epinephrine hydrochloride in the dose of 0.5 c.c. previous to arsphenamine injections, in no wise influences the occurrence of early reactive phenomena.

In a series of 101 patients atropine sulphate gr. $\frac{1}{75}$ was administered intramuscularly about ten to fifteen minutes before the arsphenamine injections, while ninety-five patients were used as controls. Both groups of patients received arsphenamine of the Dermatological Research Laboratories of the same serial number and administered under similar conditions. In the atropine series, 66 per cent. complained of various reactive phenomena. In the control series 67 per cent. experienced untoward reactive symptoms. In another group of ninety-seven patients epinephrine hydrochloride (1:1,000 solution) was injected intramuscularly in the dose of 0.5 c.c. a few minutes before the arsphenamine was administered. At first Strickler attempted to give the epinephrine intravenously, but the symptoms which developed as a result of the injection were so alarming that this method of administration was discontinued. A group of forty-two patients received arsphenamine alone. In the epinephrine series, 75 per cent. reported some untoward symptoms. In the control series, 74 per cent. had untoward results.

Arsphenamine in Stomatitis. S. Wolff⁷ praises highly the local use of a neo-arsphenamine syrup, first introduced by Patzschke in 1920 in the treatment of obstinate infective aphthous stomatitis and in Plaut-Vincent's angina, in which latter condition the local treatment may render intravenous administration unnecessary.

R

| | |
|------------------------|------------|
| Neo-arsphenamine | 0.15 c.c. |
| Syrup, to make..... | 15.00 c.c. |

Mix. Label: For local application in mouth 3 times daily.
May be used more frequently if desired.

This preparation is not only very effective, but also highly palatable, so that children actually enjoy its application, which is a great advantage when compared with the difficulty experienced in painting a sore mouth in a child with ill-tasting medicaments.

(7) Therap. Halbmonatsch., Jan. 1, 1921.

F. F. D. Reckord, and M. C. Baker⁸ also emphasize strongly the value of the local use of arsphenamine. They employ it in the form of a 10 per cent. solution in glycerine, which does not seem to disintegrate so readily as does an aqueous solution. The parts to be treated should be thoroughly cleansed and dried and then the arsphenamine solution applied by a small cotton swab and the material thoroughly rubbed into the lesions. It is surprising to see the good results obtained by applying this treatment twice a day. None of the other methods of treatment advocated has given such good results as the solution of arsphenamine. It is also indicated in those cases in which the gums are primarily involved and there is infection about the teeth as in pyorrhea, in which the authors have found fusiform bacilli and spirochetes resembling Vincent's organism in about 99 per cent. of the cases.

Neo-arsphenamine-Mercuric Chloride Combination in Syphilis. C. Tollens⁹ endorses the conjoined intravenous administration of corrosive mercuric chloride and neo-arsphenamine recently (1919) introduced by Linser. On the basis of over 2,000 injections Tollens reports better results, especially in making the patients Wassermann negative, than with previous treatment, which yielded only 35 to 40 per cent. of negative Wassermann reactions as compared with almost 75 per cent. in secondary syphilis under the new treatment. Clinical manifestations of the disease disappeared with remarkable rapidity. This treatment, furthermore, has the advantage that it does away with painful intramuscular injections of insoluble mercury salts which have hitherto been employed by preference. At first, 0.01 gm. of corrosive mercuric chloride was added to the usual solution of neo-arsphenamine, gradually the dose was increased until 0.03 to 0.04 gm. of corrosive mercuric chloride were used, together with 0.3 gm. of neo-arsphenamine in 5 c.c. of water. These injections were given twice weekly until a total quantity of 3.6 gm. of neo-arsphenamine and 0.36 to 0.48 gm. of the mercurial had been administered. Tollens has not observed

(8) Jour. Amer. Med. Ass'n., Dec. 11, 1920.

(9) Therap. Halbmonatsch., April 1, 1921.

any unfavorable results due to the mercurial addition. The fear that veins might become thrombosed by the injection of so large a dose of corrosive mercuric chloride has proved groundless, nor was embolism observed as a result of the injection of this turbid fluid. The insoluble particles in it are evidently so fine that they pass through the capillaries. As it has been shown the precipitate contains mercury and no arsenic, it is evident that in the use of this method we inject intravenously an insoluble mercurial preparation in an extremely fine state of subdivision.

Silver-Arsphenamine in Treatment of Syphilis. Silver salvarsan has been used at the Base Hospital (Station Hospital) A. E. F. in G., Coblenz, Germany, since November, 1919. Charles M. Walson¹⁰ reports that over 800 patients have been treated with it; and more than 6,000 injections given. Ampules of this substance are on the market in doses of from 0.05 to 0.30 gm. It is a greyish-black powder, which in solution takes on an ichthyol-brown color. In the intact ampule it keeps for an unlimited time; but if small cracks permit the intake of air into the ampule it becomes decomposed and poisonous. In such a state it has a darker color and does not give the ichthyol-brown solution but an opalescence of pronounced cloudiness; or it floats around on the surface of the water in black particles in which the undissolved silver salvarsan can be recognized when the solution is held to the light.

Its spirocheticidal effect is due to the arsenobenzol which anchors the arsenic into the spirochetic plasma, and to the silver which, being carried by the arsenobenzol molecule, at least restricts the multiplication of the spirochetes.

Its strength, as determined by its capacity to clear the primary manifestations of syphilis in rabbits, is twice that of old salvarsan (606) and thrice that of neosalvarsan (914). Its toxicity is less than that of "606," and perhaps not greater, if as great, as that of neosalvarsan or novarsenobenzol.

Technique of Administration: The diluent used is freshly redistilled sterilized water prepared by means of

a Jena glass apparatus and on the day of administration. All solutions are administered at room temperature. With every 0.1 gm. of the compound, 10 c.c. of diluent are used. The ampules are immersed in 95 per cent. alcohol. The proper amount of sterilized distilled water is placed in a 60 c.c. medicine glass and the contents of the ampule dropped into the diluent. The powder dissolves quickly. The solution is drawn up into a 30 c.c. Luer syringe. Prior to insertion into the median basilic vein any solution on the platinum needle is wiped off with sterile gauze to prevent irritation after making the injection. Enough blood is withdrawn to fill the syringe. This is done not only to show that the needle is in the lumen of the vein, but also because the serum reduces the toxicity of the injection. The administration requires from one to two minutes. The needle is then withdrawn quickly, the arm of the patient elevated, and pressure applied at the site of injection to prevent extravasation of fluid back into the tissues.

A board of medical officers appointed to investigate and recommend a treatment for the cure of syphilis with silver salvarsan made the following recommendations which were adopted:

An interval of seven days is observed between each dose in each course of treatment, excepting the first course, during which an interval of four days is allowed between injections.

Treatment should consist of four courses of silver salvarsan and gray oil. In the first course of treatment the first dose should be 0.15 gm. of silver salvarsan; second dose 0.2 gm. of silver salvarsan; and each of the remaining five doses of the first course 0.3 gm. of silver salvarsan.

At the end of the first course of treatment, a Wassermann blood test should be made and then thirty days' rest allowed.

In the second course of treatment 0.3 gm. silver salvarsan is given for each dose, with seven-day intervals, then two and a half months' rest; the course to consist of seven doses.

The third course is the same as the second with ninety

days' rest. The fourth course is the same as the second or third course.

In conjunction with and at the time of each injection of silver salvarsan 0.08 gm. gray oil should be given intramuscularly. A Wassermann blood test is recommended after each course and a spinal fluid examination after the second course. During the second year of the disease every three months a Wassermann blood test and lumbar puncture should be made with a complete serologic examination of the spinal fluid. If at any time the Wassermann blood test becomes positive, treatment should be renewed. If at the end of the twenty-fourth month the Wassermann blood test and spinal fluid are negative, the case is considered cured.

Results in Primary Syphilis: Where the primary lesion has existed for less than fifteen days, apparently complete abortive cure occurred in from 80 to 100 per cent. of all cases, provided that the patient presented himself when only the dark field examination was positive, but the Wassermann negative.

Results in Secondary Syphilis: Out of 516 cases, 70 per cent. were Wassermann negative at the end of the first course; 25 per cent. negative at end of second course; 5 per cent. negative at end of third course.

Clinical Effects: Forty-eight hours after the injection of 0.15 gm. of the silver salvarsan plus 0.08 gm. of the gray oil, no spirochetes were found in the initial lesion. The effect of the treatment on all grades of syphilis has been found to be favorable. The best results, however, are obtained in all the cases showing the ordinary clinical signs of secondary syphilis, with mucous patches in the mouth and throat and the exanthemata, all of which are eliminated as rapidly as after treatment with the older salvarsan preparations.

Effect on Later Manifestations of Syphilis: Silver as a colloid or crystalloid alone has been found effective in cerebral syphilis and in tabes. Its effect is not lost when in combination. Silver salvarsan has been given with remarkably good results in some cases of interstitial keratitis.

Untoward effects are sometimes seen after silver salvarsan. Anaphylactoid symptoms have followed espe-

cially the first administration of each course. Therefore, the first dose of each fresh series of doses should be given very slowly and in small amounts to overcome the oversensitiveness. Angioneurotic symptoms have not been very serious. Not a single death has occurred during the 100,000 injections. Perhaps in some cases the concentration of the solution must be reduced to about 1 per cent. Spirochete fever is not uncommon in primary and secondary cases, giving a rise in temperature after the first injection. If there is an increase of temperature after the second and third injections, the treatment must be delayed. Any arsenobenzol preparation may have much the same effect in late primary or early secondary syphilis; this is probably due to the sudden throwing out into the circulation of the protein products of the breaking down spirochetes.

Neuro-relapses: Although there is some tendency of local spreading of the spirochetes liberated from their foci by the action of the drug, yet very few nervous relapses have been reported. However, it has been found that such might occur more frequently than after neo-salvarsan or novarsenobenzol.

Periphlebitis rarely occurs and then only after faulty technique leading to extravasation of the solution into the tissues at the site of injection, or from trauma of the vein. No cases of *argyria* have yet followed the courses in the army hospitals and none has been reported in the literature.

Mihran P. Parounagian¹ has used silver arsphenamine, which in reality is the sodium salt of silver arsphenamine, in 4,290 administrations to 756 patients. All stages of syphilis have responded to this treatment with gratifying rapidity and thoroughness. His impression is that the response begins more promptly and that the lesions resolve with greater rapidity than is the case with a similar number of treatments with other arsenical preparations.

Technique for Administration of Silver-Arsphenamine, R. L. Cowen² finds that an extravasation of a little silver-salvarsan into the tissues is more disastrous than

(1) Jour. Amer. Med. Ass'n., Nov. 26, 1921.

(2) Amer. Med., August, 1921.

following any other form of arsphenamine. A frequent untoward occurrence following the injection of silver-salvarsan is a small nodule in the vein at the site of injection. This can always be attributed to a slight infiltration of the drug into the vein wall itself, which may easily occur when the vein is being entered and a small drop of the solution forced into the media of the vein. It very frequently happens that the plunger of the syringe slides down by its own weight during the act of entering the vein, and injects a drop of the fluid into the vessel wall without the physician being cognizant of the fact. In order to obviate this, Cowan advises fixation of the plunger by the thenar eminence to control injection until the needle is absolutely within the vein lumen (Plate I.)

Solutions of silver-salvarsan in 5 c.c. cause no local phlebitis if care be maintained that an intramural injection does not occur; but a dilution of 15 c.c. is just as convenient. Frequent aspirations of blood into the syringe during the injection not only serve to indicate that the needle is still in the vein lumen, but also give a better diluent for the drug than water. A routine method for alternation of aspirations with injection is to inject 2 c.c., withdraw 1 c.c., inject 2 c.c. more and again withdraw 1 c.c. of blood, and so on until completion. This gives a dilution of about 10 c.c. of blood, which forms, apparently, a colloidal silver-salvarsan solution, the best prophylactic against unfavorable reactions. This method is not suitable for "Neo," or old arsphenamine as these are not freely miscible with blood.

Sulfarsenol in Congenital Syphilis. E. Crawford and G. B. Fleming³ have treated thirty-five children with sulfarsenol—a drug which can be given intramuscularly without causing either pain or sloughing. In order to compare the results with those published for kharsivan the children have been divided into two groups: (1) children under 1 year of age; and (2) children over 2 years of age. Group I, (nineteen children) received from seven to nine injections and a negative Wassermann reaction was obtained in eight, or 42 per cent. The figures given by Dr. Findlay for kharsivan indicate much

(3) *Lancet*, Oct. 1, 1921.

better results. A negative Wassermann reaction was obtained in 64 per cent. of his cases after a course of nine or fewer injections. In Group II, of twelve children over 1 year old none gave a negative Wassermann reaction after from three to fifteen injections of sulfarsenol, whereas among Dr. Findlay's patients over 1 year old treated with intravenous injections of neokharsivan a negative Wassermann reaction was obtained in 50 per cent.

These results suggest that the intramuscular injection of sulfarsenol is not so efficacious in producing a cure of congenital syphilis, as evidenced by the Wassermann reaction, as is intravenous injection of kharsivan.

QUININE

Destructive Action of Quinine on the Tissues. L. S. Dudgeon,³ as a result of an experimental study, arrives at the conclusion that injection of quinine in solutions so dilute as to avoid edema and tissue necrosis is not of practical utility in man. Preparations of quinine concentrated enough to be of therapeutic value also excite necrosis at the point of injection. Such solutions are absorbed rapidly from the tissues even in patients who are moribund. No advantage was gained by the addition of oil or by injecting the alkaloid dissolved in alcohol or ether. Necrosis of blood-vessels in the area of injection is a common result. This leads, according to Dudgeon, to hemorrhage into the tissues. Extensive damage of this kind in the neighborhood of an important nerve trunk may result in nerve palsy.

Daily doses administered for periods of a week and more in the gluteal region may leave only fragments of healthy tissues in the muscular tracts involved. Hence, repeated intramuscular injections of quinine should not be given into the same area of muscle, or tissue directly adjacent, because otherwise permanent injury of muscle or nerves may result.

Dilute Solution of Quinine for Intravenous Injection. U. N. Brahmachari⁴ recommends the use of very dilute solutions of quinine for intravenous injection in malaria,

(3) Jour. Amer. Med. Ass'n., Feb. 14, 1920.

(4) Indian Med. Gaz., December, 1920.

preferably a 1 to 300 dilution. In malaria, especially the pernicious type, the blood-pressure is generally low. Intravenous injection of quinine in concentrated solution (0.65 gm. to 20 c.c.) is generally followed by a fall in blood-pressure and sometimes by a disappearance of the pulse for a few seconds. Intravenous injection of quinine in dilute solution (0.65 gm. in 200 c.c.) may be followed by a fall in blood-pressure, but it is neither so sudden nor so great as in the case of concentrated solutions. The slower the injection the less the fall of blood-pressure. The injection is best given at the rate of 10 c.c. a minute. The lowered blood-pressure may persist for twelve hours or more after injection. In case alarming symptoms appear during the injection, the administration of pituitary extract or epinephrine and the application of tight bandages over the extremities should be resorted to.

Antagonistic Action of Quinine and Epinephrine.

By experiments upon dogs, A. Clerc and C. Pezzie⁵ found that quinine causes a rapid fall of blood-pressure with momentary decrease in cardiac activity followed by a compensatory increase with a gradual return to normal. When, at the point of greatest activity of quinine, epinephrine is administered it is without its characteristic effect upon blood-pressure even when given in double doses. On the basis of these experiments, the authors arrive at the conclusion that quinine depresses the sympathetic nerve centers and stimulates the vagus centers. Epinephrine strengthens and accelerates cardiac action; quinine depresses it without producing depression of the muscle, however, for in the dose under consideration, quinine acts as a muscular stimulant. This explains the mode of action of quinine in conditions of excessive action of the sympathetic nervous system.

The Quinotoxin Myth. Some writers, especially in chemical and pharmaceutical journals, have attributed the toxic effects of quinine to the formation of a more toxic substance, "quinotoxin," or quinicin, as it is more properly called, which may be formed from quinine under suitable conditions, especially in the presence of free organic acids. It has been assumed that these conditions

(5) Jour. de physiol. et de pathol. gén., December, 1920.

would arise in the stomach, and, also, that prescriptions containing quinine and an organic acid would be dangerously incompatible. T. Sollmann⁶ shows by an examination of the data that these fears are not justified by the facts; that at most insignificant traces of quinotoxin could be formed in the body or be present in such prescriptions, and that the formation of considerable quantities would not be dangerous. The error arose originally from exaggerated conceptions of the toxicity of quinotoxin, and was fostered by unproved assumptions as to the amounts that might be formed under practical conditions.

“Quinotoxin” (more properly, quinicin) may be formed in prescriptions containing quinine and organic acids; but this proceeds very slowly, and the quinicin undergoes further transformation into inactive products. Such solutions are perfectly proper if used within a few days. They should not be used after prolonged standing, when they become discolored and precipitated; not because they have become toxic, but because they have become inactive.

ETHYLHYDROCUPREINE

Progress in the Use of Ethylhydrocupreine (Optochin). The remarkable specific action of this drug⁷ *in vitro* against the pneumococcus, which it kills in solution as dilute as 300,000 has thus far met the hopes it aroused only in pneumococcus infection of the cornea (*ulcus corneae serpens*) in which condition a collyrium of 0.5 to 1 per cent. solution has been found very effective. Its employment in pneumonia has given rise to contradictory reports. This may be due in part to the intrinsic difficulty of bringing undisputable proof by the statistical method, still the most that can be said in its favor is that it seems to have produced favorable results upon the fever and the subjective sensation of patients in whom the treatment was used sufficiently early. There is, however, no doubt regarding the dan-

(6) Jour. Amer. Med. Ass'n., April 9, 1921.

(7) Practical Medicine Series, 1916, Vol. VIII.

ger of this remedy by reason of its unfavorable effect upon the optic nerve, which is liable to result in either transient or permanent blindness. Up to three years ago, about sixty cases of such occurrence had been reported. Of late very few cases have been published. It may be that this is due to several improvements in the technique of the use of this drug that have been developed within the last few years and which have lessened the danger. Nevertheless, the remedy is still dangerous and should be employed only in hospitals under constant and careful supervision.

This subject is also discussed by G. A. Waetzoldt,⁸ who states that the visual disturbances following optochin are essentially due to errors in dosage and the use of an unsuitable preparation, the easily soluble, rapidly absorbing hydrochloride of optochin. He believes that optochin hydrochloride should be eliminated from pneumonia therapy except for intravenous injections, for which purpose, not more than a total of 0.6 gm. should be given in twenty-four hours, divided into equal doses administered at six-hour intervals. Only the slowly soluble basic optochin (dose, 0.25 gm.), or the still less soluble optochin salicylate (dose, 0.30 to 0.40 gm.) should be employed, and the dose repeated not oftener than every six hours. To minimize the formation of soluble hydrochloride in the stomach, it is desirable to use a diet that excites the hydrochloric acid secretion of the stomach to a minimal degree, or to employ an alkali to neutralize the gastric acid. At the first sign of unfavorable by-effects, such as ear or eye disturbance, the administration of the drug should be stopped immediately.

For children, the author recommends the subcutaneous administration at six-hour intervals of the number of years of the child's age multiplied by: 0.015 gm. basic optochin or 0.020 gm. optochin salicylate.

The basic optochin may be administered in oily solution subcutaneously in practically the same dosage as by mouth.

The intraspinal use of optochin in pneumococcus meningitis is unobjectionable, Waetzoldt says, so far as dan-

(8) Therap. d. Gegenw., 1921, p. 96.

ger of visual disturbance is concerned. The dose ranges between 0.06 to 0.08 gm. in 3 to 1,000 solution.

For children one-tenth the adult dose may be used in the same concentration.

Ethylhydrocupreine in Experimental Pneumococcus Meningitis. J. A. Kolmer and G. Idzumi⁹ show that in mixtures of equal parts of purulent spinal fluid and from 1:1,000 to 1:2,000 solutions of ethylhydrocupreine complete destruction of very large numbers of virulent pneumococci occurred within one hour at 37° C. The intrathecal injection of 0.5 c.c. of 1:500 and 1:1,000 solutions per kilo of body weight, when administered not later than from four to six hours after the injection of culture, had a distinct beneficial effect on the course of experimental meningitis in rabbits produced by Type I pneumococci. The drug was probably diluted in the subarachnoid space by 1 or 2 c.c. of spinal fluid per kilo, giving final dilutions of 1:2,000 to 1:5,000; these dilutions of drug, however, apparently showed some pneumococidal activity even in the presence of inflammatory exudates, and were found to have no irritative effects for the meninges. Furthermore, since the amount of drug injected at one time was 0.5 c.c. of a 1:500 dilution per kilo of weight, or 0.001 gm., it was less than the toxic dose by intrathecal injection; this permitted the administration of multiple doses without toxic effects.

Ethylhydrocupreine in Experimental Pneumococcus Pleuritis. J. A. Kolmer, and J. R. Sands¹ reaffirm the high selective pneumococidal activity of ethylhydrocupreine by finding that creamy pleural pus containing Type I pneumococci mixed with an equal part of 1:1,000 solution of ethylhydrocupreine was completely sterilized in about thirty minutes. Whereas, portions of the same pus heavily inoculated with a laboratory culture of *staphylococcus aureus* in mixtures of equal parts of pus and 1:1,000 solution of ethylhydrocupreine showed no appreciable diminution of the staphylococci after exposures as long as two hours, although the pneumococci were destroyed. Since pleural pus is ordinarily much richer in pus cells than meningeal pus it required

(9) Jour. Infect. Dis., April, 1920.

(1) Jour. Exper. Med., June, 1921.

PLATE I.



A. A firm grasp on the syringe with the index finger, parallel to the vein, resting on the shaft of the needle. The plunger of the syringe is fixed by the thenar eminence. (The left index finger or thumb is used to fix the vein from sliding.)



B. Shows grasp, which is maintained from start to completion, on the syringe.



C. Left hand resting on patient's arm; left thumb is used for injecting. Right hand is not moved from the original position.—Cowen, page 40.

stronger dilutions of ethylhydrocupreine to effect complete destruction of large numbers of pneumococci. Guinea-pigs and dogs, however, show no ill effects from the intrapleural injection of 1 c.c. of 1:500 ethylhydrocupreine per kilo. Such doses were at least two and one-half to five times less than the toxic doses. The injection of 1 c.c. of a 24-hour dextrose blood-broth culture of virulent Type I pneumococci into the right pleural cavity of guinea-pigs produces acute suppurative pleuritis on both sides associated with suppurative pericarditis, which generally terminates fatally within seventy-two hours with pneumococcus bacteremia. The injection of 1 c.c. of 1:500 solution of ethylhydrocupreine hydrochloride into each pleural cavity of guinea-pigs at varying intervals up to twenty-four hours after pleural infection has usually shown a marked curative influence. Similar results were observed with dogs.

It is evident that certain drugs may be injected into serous cavities in amounts exerting distinct bactericidal activity *in vivo* without producing local irritation or general toxic effects, when their introduction in sufficient quantities into the blood stream would be impossible.

CHAULMOOGRA OIL

History and Present Status of Chaulmoogra Oil Therapy. This is well presented in an article by L. E. Warren² from which we abstract the following data.

Chaulmoogra oil has been used in India and adjacent countries both orally and externally in the treatment of leprosy since prehistoric times. However, it is so irritant to the intestinal tract that the oral dosage can seldom be pushed to the curative point. On hypodermic or intramuscular administration it is not only painful but, being a heavy oil, is slowly absorbed. It was long supposed that chaulmoogra oil was derived from the seeds of *Gynocardia odorata*. It is now known that the true source of chaulmoogra oil is the seeds of *Taraktogenos kurzii* (*Hydnocarpus heterophyllus*) a handsome tree of Burma. The fruit of *Taraktogenos* is of the

(2) Jour. Amer. Pharm. Ass'n., July, 1921.

size of a grape fruit, and it contains many irregular-shaped, brown seeds, which are rich in oil. Chaulmoogra oil obtained from these seeds by cold expression is at ordinary temperatures a soft solid or semi-solid liquid, having a peculiar, characteristic odor somewhat like linseed oil.

It was shown in 1904 by Powers and his associates that the oil consists chiefly of glyceryl esters of two or more fatty acids (Fig. 8), which differ from any previously known fatty acids in containing a five-membered carbon ring. Also,

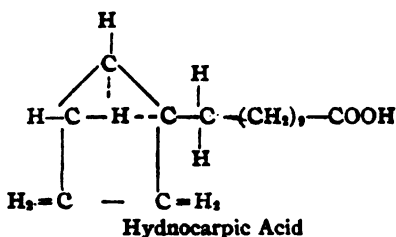
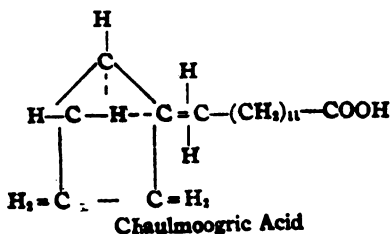


Fig. 8. Constitution of the Acids of the Chaulmoogric Series.
 $C_nH_{2n-4}O_2$

probable that the specific bactericidal and medicinal properties of these acids are associated in some way with their molecular constitution. The oil from *Gynocardia odorata* is totally unlike the oils from the chaulmoogra series of plants, and from its constitution it is probable that gynocardia oil can not be of any value in the treatment of leprosy. It is reasonable to suppose that oils from other plants will be found to contain chaulmoogric acid and its homologues.

Leonard Rogers (1916) used a mixture of the separated fatty acids of chaulmoogra oil, which he called collectively "gynocardic acid," in the form of the sodium salts subcutaneously, and later intravenously, with great improvement and even cures in 50 per cent. of the cases treated within three years of the onset of

the disease. In those of longer duration only 25 per cent. cleared up. The results being still not entirely satisfactory, Rogers and Mukerjee (1919) used "sodium hydnocarpate" with results which they consider very promising.

Walker and Sweeney (1920) found by bacteriologic methods that chaulmoogric and hydnocarpic acids were about 100 times more active than phenol against the acid-fast group of bacteria, and inactive against all other bacteria tested.

In 1918, Hollmann and Dean at the U. S. Leprosy Investigation Station in the Hawaiian Islands commenced the employment of the ethyl esters of the fatty acids from chaulmoogra oil which are thin liquids soluble in water, thus lending themselves to use by subcutaneous, intramuscular, and intravenous injections. They were chiefly employed by intramuscular injection. The work of Hollmann and Dean at the Hawaiian Station was continued by McDonald who administered the esters combined with 2 per cent. of iodine, which he later admitted was not essential. He also employed the fatty acids internally but later decided that oral administration was not necessary. With an average treatment lasting fifteen months, seventy-eight patients were paroled from the station between October 1, 1918 and July 6, 1920. In a later report, McDonald states that of a total of one hundred, forty-two patients have been paroled as no longer a menace to public health, not one of whom has suffered a relapse.

It will be seen that at present there are two relatively distinct systems of treatment for leprosy with chaulmoogra oil. One of these is now chiefly championed by McDonald and Dean who use principally the mixed ethyl esters of the fatty acids of chaulmoogra oil by deep intramuscular injection. The other system is represented by Rogers and his followers in India who chiefly use the sodium salts of the fatty acids of chaulmoogra oil, for the most part intravenously. It would appear that the results obtained by the American school represent the larger percentage of clinically cured cases.

All leprosy workers agree that the treatment with chaulmoogra derivatives is tedious alike for patient and

physician. The physician must keep on driving at the treatment until the patient dies or recovers. Hence the only place for carrying out this treatment is a leprosy hospital where association with and observation of fellow patients, leads to continuance of an otherwise discouraging therapy. The value of hygiene, good food, and an open air life is emphasized by all clinicians.

The present situation may be summarized as follows: Although results indicate that derivatives of chaulmoogra oil are almost specific in the treatment of leprosy, yet among the many clinicians there are none, with the possible exception of McDonald, who has been willing to assert dogmatically that leprosy can be cured. While the outlook for permanent cure in many cases seems to be distinctly hopeful, there will always remain some cases that will prove intractable; and, as some cases will continue to escape segregation, so that the spread of the infection will not be stopped, the entire disappearance of leprosy from the face of the earth, as has been prophesied, is not likely to be realized during the lifetime of any now living.

Chaulmoogra Oil in Leprosy. J. T. McDonald, and A. L. Dean³ report a study of the effect of the constituents of chaulmoogra oil in leprosy. The fact that 50 per cent. of the patients who have been in the hospital during the period from January 1, 1920, to March 15, 1921, have recovered shows that we now have methods in hand for holding the disease under control.

The two unique unsaturated fatty acids, chaulmoogric and hydnocarpic acids, converted into their ethyl esters, were used. Of ten unselected patients, the first five were given weekly intramuscular injections of the ethyl ester of chaulmoogric acid; the second five were given injections of the ethyl ester of hydnocarpic acid. All the patients have shown improvement, two of those receiving chaulmoogric acid have been paroled after less than a year of treatment, and three of the patients on hydnocarpic acid have been paroled. Six still remain in the hospital. The results obtained with those patients who have received no chaulmoogra oil or its derivatives by way of mouth, but have received injections of the

(3) Jour. Amer. Med. Ass'n., May 28, 1921.

ethyl esters, have shown conclusively that the oral administration is by no means necessary. When chaulmoogra oil was given only by mouth, not only was there intolerance of the oil taken this way, but even with those patients who were able to retain the oil, its effects were slow and uncertain; so that, although chaulmoogra oil was regarded for many years as a useful drug in the treatment of leprosy, it was by no means considered as a satisfactory remedy or one that could be relied on. The auxiliary use of oral administration is therefore of doubtful utility.

The authors incline to the view that hydnocarpic acid is more effective than chaulmoogric acid; and suspect that, as one goes down in the chaulmoogric acid series, the acids of lower molecular weight will prove more active. The patients have received no iodine, and did not appear to have suffered from its absence. Hence, the rôle of the iodine in the "standard treatment" is at most a minor one. In the clinical use of the remedies one of the most serious handicaps is the tendency to eruptions which certain patients show. Something like 10 per cent. of the patients are unable to take injections continuously, because they tend to break out with swellings which may perhaps be a form of toxemia, or may be an anaphylactic reaction. The control of this reaction is therefore highly desirable and offers a field for further investigation.

MISCELLANEOUS ANTISEPTICS

Picric Acid as Skin Disinfectant. As a result of comparative experiments and clinical experience, H. W. Hewitt³ advocates, in emergency cases, a dry shave, followed by scrubbing with ether for three minutes, and then with a 6 per cent. picric acid solution in ethyl alcohol for three minutes. In other cases, shaving and scrubbing with soap and water should precede operation by from twelve to twenty-four hours. The method of preparation is simple, cheap and efficient. It does not injure the skin or even the peritoneal coat of the intestine.

(3) Amer. Jour. Obstet. and Gynec., April, 1921.

C. E. Farr⁴ likewise considers picric acid ideal as a skin disinfectant. The 5 per cent. solution can be applied anywhere except to the conjunctiva. Its only drawback is its very striking color.

Intravenous Use of Antimony Tartrate in Tropical Diseases. J. B. Christopherson's⁵ experience seems to show that antimony tartrate (0.3 to 0.5 gm.) by intravenous injections may be sufficient to cure leishmaniasis of the skin, more (1.3 to 2.0 gm.) is necessary, as a rule, to bring about a cure in bilharziasis, and still more (4 gm., perhaps, and more) is required for leishmaniasis or kala-azar, and possibly still more (probably in repeated courses) for the cure of trypanosomiasis. Antimony tartrate (the double salt with potassium or sodium) when given intravenously in appropriate dilution and administered with care may be given in larger doses than is generally supposed.

H. B. Day⁶ reports an analysis of 100 cases of bilharziasis with, on the whole, satisfactory results. To adults was given an initial dose of 0.06 gm., the next time 0.09 gm. and on each subsequent occasion 0.12 gm. at a dose in rather concentrated (6 per cent.) solution. Not many out-patients could take a larger dose without suffering from persistent giddiness and often vomiting. Young women and youths generally took 0.09 gm. as a full dose, and it was found that many children could tolerate this amount. The injections were given as a rule on alternate days. In order to achieve a permanent cure at least 0.85 gm. of antimony tartrate is necessary, though still larger amounts are desirable. Some cases required over 2 gm. The effect of antimony is primarily exerted upon the ova themselves, and they become shriveled and blackened. Upon the parent trematodes the action of the drug is cumulative, and does not take effect till a total of 0.65 gm. has been administered. Treatment must be continuous, for if interrupted for any length of time the parasites are given a chance of recovery from the primary intoxication.

(4) *Ann. Surg.*, January, 1921.

(5) *Lancet*, March 12, 1921.

(6) *Ibid.*

Camphorated Phenol. M. Herrmann⁷ calls attention to the value of "Chlumsky's solution" as an application to infected wounds in which it displays gratifying antiseptic and analgesic action. Chlumsky in 1905 recommended the following prescription in the treatment of erysipelas and other local infections such as felons and furuncles:

℞

| | |
|----------------------|--------|
| Phenol | 30.00 |
| Camphor | 60.00 |
| Alcohol to make..... | 100.00 |

H. Wieland⁸ points out that the remarkably slight damage to tissue produced by so concentrated a solution of phenol is due to the fact that camphor is an excellent solvent for phenol, while water dissolves it very poorly. The camphor in this combination merely plays the mechanical rôle as an oily solvent for phenol. In a wound this oily solution gives off phenol very slowly until an equilibrium is reached, which is conditioned by the solution of phenol and camphor on the one hand, and in the wound secretion on the other. Hence, the concentration in the wound always remains low; but is maintained at a constant level by its application.

W. Heubner reminds us that like camphor, free alkaloids such as cocaine and atropine, almost completely annihilate the corrosive action of phenol.

Menthol and Eucalyptus Oil Injection in Febrile Tuberculosis. Gerty and K. Cori⁹ report satisfactory results in the treatment of febrile tuberculous patients in whom tuberculin treatment was contraindicated, with a modification of Berliner's injection (1905). They use the following formula:

℞

| | |
|------------------------|-----------|
| Iodine | 0.1 gm. |
| Camphor | 0.5 gm. |
| Menthol | 10.0 gm. |
| Oil of eucalyptus..... | 10.00 gm. |
| Castor oil | 20.00 gm. |

From 0.5 to 1 c.c. injected intramuscularly two or three times weekly.

(7) Therap. Halbmonatsh., July 1, 1921.
 (8) Ibid., July 1, 1921.
 (9) Ibid., April 15, 1921.

These injections are made between the anterior superior spine of the ilium and the trochanter. A special syringe is reserved for this purpose which, as well as the needle, need not be boiled or disinfected, as the fluid is sufficiently disinfectant. The injections only occasionally cause pain which may extend down the leg and last for twenty-four hours. Kidney irritation was not observed, though the urine should be examined before the injections as albuminuria would constitute a contraindication. Intravenous injections must be carefully avoided, as they may have been responsible for an occasional feeling of depression noted by some clinicians.

The authors used these treatments in a series of 168 cases and found the effects much better and more reliable than treatment with the iodine-guaiacol injections of Contani. Of fifty patients belonging to the second stage (Turban's) of pulmonary tuberculosis, only 4 per cent. were not relieved of their fever by injections numbering from one to twenty-four. Among eighty-five in the third stage, about 52 per cent. were relieved of fever, by from one to twenty-four injections, the total number used ranging from two to forty-two. This shows that the effect of these treatments is less marked in the more advanced cases. However, even in the last stages of tuberculosis, these injections are of value inasmuch as they lessen many of the symptoms, such as pain, dyspnea, night sweats, cough, and expectoration. The deodorizing effect of the remedy which is partially eliminated through the expired air is also grateful. Many times, patients were able to sleep after these injections when previously they required codeine to induce sleep. Patients who developed fever after sun baths were found able to take these baths without such effect after these injections. There is likewise a diminution in the tendency to fever on exertion.

When fever develops in the course of tuberculin treatment these injections checked the fever and permitted a continuation of the tuberculin treatment.

The mode of action of these injections is not to be thought of as merely antipyretic, in view of the fact that the reduction of temperature lasts a good deal longer than would be possible on the basis of antipyretic action.

The effect must be due to some influence upon the tuberculous foci in the lungs, which is rendered probable by the demonstrated accumulation of volatile oils in the lungs (Mansfeld, 1918), and by the influence which volatile oils have been shown to possess upon inflammatory processes in the system. This action is by no means specific for tuberculosis, but is also demonstrable in chronic bronchitis where volatile oils have a well-established reputation as expectorants and in influenza pneumonia, where numerous authors believe they have obtained good results from their use, especially in those cases with prolonged course.

To investigate the question whether the injections act upon the tuberculous foci in the lungs so as to lessen the degree to which they discharge pyrogenic and other poisons into the circulation, the authors studied the effect of this treatment upon the von Pirquet reaction in seventeen patients, with the result that it became distinctly diminished in 70 per cent. of the cases and in half of these even negative as a result of injections ranging from five to twenty-six in number. However, this diminution of the von Pirquet reaction is merely temporary and from four to nineteen days after the last injection the response becomes greater again and may even be equal to the first reaction. This transient diminution of the von Pirquet reaction is in marked contrast to its prolonged lessening for the course of many years that occurs as the result of a course of tuberculin treatment.

The menthol-eucalyptol injections are, therefore, only advocated by the authors in those cases in which fever (rectal temperature above 37.7° C.) contraindicates the use of tuberculin.

Administration of Emetine Bismuth Iodide. Geo. E. Ewe⁹ discusses this compound, which has given favorable results in the treatment of endamebiasis. It is probably an adsorption compound and not a true chemical combination, as a large number of experiments failed to produce a compound which would not yield alkaloid upon washing with water. However, the rate of liberation of the alkaloid is so slow as to make this

(9) Jour. Amer. Pharm. Ass'n., April, 1921. Digitized by Google

combination infinitely superior to emetine hypochloride and ipecac preparations for oral administration. It should never be dispensed as an ingredient of a liquid preparation, since it would be partially decomposed with the liberation of a soluble emetine salt and would therefore more readily cause nausea. By far the most favored method of administering it at present is in the form of the powder enclosed in cachets or capsules. However, the molded tablet readily disintegrates and is quite practical.

Acridiflavine in Otitis Externa. J. Coleman Scal¹⁰ reports a series of seventeen cases in which the process has been arrested with one application if the patient was seen early; while, in well-developed cases, three applications have sufficed. The method of treatment consists in first cleansing the ear canal with dry cotton applicators, then packing the canal tightly with gauze strips, saturated with 1:1,000 solution of acridiflavine, being careful not to pack too near the drum. This packing tends to stretch the canal and permits the antiseptic to act on all the microorganisms in the crevices and fissures. The patient is supplied with some of the solution and ordered to keep the packing moist by the use of a medicine dropper. This procedure is repeated every twenty-four hours, until the ear canal is completely patulous and free from infection and pain. One week is the usual length of time required to clean up an infection. In cases in which definite furuncles have formed or are forming, when the packing is removed, the furuncles will be found to have opened themselves and the pus to have been absorbed by the gauze. In this treatment incision of the furuncles is avoided and the length of the process is remarkably shortened.

Aniline Dyes in Ophthalmology. W. Löhlein,¹ who with Römer and Gebb has for many years examined the effect of various aniline dyes against different microorganisms has found a marked specificity of various dyes against certain microorganisms which he tabulates as follows:

(10) Jour. Amer. Med. Ass'n., Oct. 1, 1921.

(1) Therap. Halbmonatsh., Sept. 15, 1921.

- Against Pneumococci: Azoflavin, Chrysoidin, Methylene Blue, Rose Bengale, Victoria Yellow.
- Against Staphylococci: Brilliant Green, Gentian Violet, Iodine Green, Malachite Green, Methylene Violet, Methyl Violet.
- Against Xerose Bacilli: Hoffmann's Violet, Magdala Red, Malachite Green, Methylene Violet, Methyl Green, Methyl Violet 3 B., Saffranin, Victoria Yellow.
- Against Diplobacillus of Morax-Axenfeld: Brilliant Green, Gentian Violet, Hoffmann's Violet, Magdala Red, Malachite Green, Methylene Blue, Methylene Violet, Saffranin, Toloidin Blue.
- Against Streptococci: Brilliant Green, Malachite Green, and Victoria Blue.
- Against Gonococci: Brilliant Green, Brilliant Black (Variable), Chrysaniline, Hoffmann's Violet, Iodine Green, Malachite Green, Methylene Blue, Methylene Violet, Methyl Green, Methyl Violet 3 B., Saffranin, and "Säuregrün."

To make use of this knowledge in practice it was next necessary to determine the maximum concentration tolerated by the human eye and the lowest concentration that still displayed bactericidal action. In this work it was found that occasionally strains were encountered that were unusually resistant to a certain agent. This led to the idea of the desirability of combining, as much as practicable, the various agents that have been found useful against a certain species of bacteria, in order to increase bactericidal action without increasing undesirable by-effects. This led to the following combinations of dyes:

1. *Dyes Effective Against Pneumococci.*

| | Concentration |
|-----------------------|---------------|
| Rose Bengal | 1: 25 |
| Azoflavin | 1: 200 |
| Victoria Yellow | 1: 200 |

2. *Dyes Effective Against Diplobacillus Morax-Axenfeld (also Staphylococci, Streptococci, and Xerose Bacilli.)*

| | Concentration |
|-------------------------|---------------|
| Brilliant Green | 1: 1,000 |
| Hoffmann Violet | 1: 1,000 |
| Malachite Green | 1: 1,000 |
| Methyl Violet 3 B. | 1: 1,000 |
| Saffranin | 1: 500 |
| Magdala Red | 1: 500 |
| Toluidin Blue | 1: 500 |

3. Dyes Effective Against Gonococci.

| | Concentration |
|-------------------------|---------------|
| Brilliant Green | 1: 5,000 |
| Gentian Violet | 1: 200 |
| Hoffmann Violet | 1: 200 |
| Iodine Green | 1: 400 |
| Malachite Green | 1: 600 |
| Methylene Blue | 1: 100 |
| Methyl Violet 3 B. | 1: 200 |

To combine these three into one mixture is impossible as acid dyes that are effective against pneumococci could not be mixed with Groups 2 or 3.

These mixtures have now been used for nearly ten years in the clinic at Greifswald with excellent results in infectious conditions of the eyelids and conjunctiva. However, since the introduction of optochin the mixture against pneumococci has not been employed to any great extent. Similarly, the mixture against gonococci has been displaced by experiments with proteotherapy. However, the dye mixture in Group 2, which is specifically useful against the diplococci Morax-Axenfeld, must be considered an important contribution to progress in this obstinate form of conjunctivitis which can be cured by treatment with this mixture within a few days. It is desirable to rub an applicator dipped in the mixture against the margin and angle of the lids as it is here that the secretion swarming with bacteria usually adheres most tenaciously. Besides this, the solution should also be dropped into the eye. The treatment is applied once or twice a day, and over night a corrosive sublimate salve or a salve containing the dyes is applied. The staining qualities of this mixture which might seem objectionable are not usually objected to by the patient, who willingly accepts the slight transient blue discoloration of the conjunctiva in exchange for a rapid cure of the distressing affliction. For the physician the discoloration is of some advantage as he can recognize thereby that the dye has been applied to all parts of the conjunctival sac. Practice soon makes one perfect in avoiding the spilling of the pigment solution over the cheeks. It is only in superficial processes that good results may be expected. Deep infections are not likely to be benefited.

Löhlein also calls attention to the value of scarlet red salve in the treatment of corneal erosions. He employs it in the following manner:

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| | |
|--|----------|
| Scarlet red | 5.00 gm. |
| Olive oil enough for trituration to finest possible particles. | |
| Petrolatum to make..... | 100.00 |

To obtain the stimulation of epithelium by means of this remedy it is necessary to produce an increased pressure within the tissues. This may be obtained by means of a pressure bandage applied to the eye. Often within a day the corneal surface becomes smooth and shiny. Nevertheless, it is desirable to continue the treatment for at least five and not more than eight days after which it is best to use for many months the nightly application of boric acid ointment to the conjunctival sac. The author warns against using this remedy in infectious processes, as it has no bactericidal power whatever.

ANTHELMINTICS

Oil of Chenopodium in Hookworm Disease. S. T. Darling and Wilson G. Smillie² studied four groups of patients to determine (1) the influence of the preliminary purge, (2) the influence of the preliminary starvation, and (3) the influence of food given during the treatment. They conclude:

A preliminary purge does not add to the efficiency of the treatment with chenopodium, when the drug is given in two doses of 0.75 c.c. each (1.5 c.c. being considered the adult dose).

A preliminary starvation period is not necessary in the treatment of hookworm disease with chenopodium in divided doses of 1.5 c.c.; but, on the contrary, the efficiency of the drug is lessened.

A small amount of food given coincidentally with the drug, when the chenopodium is given in divided doses, greatly diminishes the efficiency of the drug.

In the smaller doses of chenopodium that are given to

(2) Jour. Amer. Med. Ass'n., Feb. 12, 1921.

children the decrease in efficiency of the drug caused by the preliminary purge, the starvation period and the food is much more striking than in the full adult dosage of 1.5 c.c.

Carbon Tetrachloride in Hookworm. M. C. Hall³ advocates a trial of this drug on the basis of very gratifying results on dogs when these animals were given 0.3 c.c. of this drug for every kilogram of live weight—a dose of 3 c.c. for an average sized (10 kg.) dog. All the hookworms originally present were expelled, a result Hall has never been able to obtain in any series of tests of anthelmintics on hundreds of dogs during the last six years. Among the drugs previously tested were thymol, chenopodium, chloroform, and combinations of chenopodium and chloroform. The carbon tetrachloride is also very effective in removing ascarids, being only slightly less effective than chenopodium, which in experiments proved practically 100 per cent. effective in removing ascarids from dogs, when given in doses of 0.1 c.c. per kilogram of live weight and immediately preceded or followed by 30 c.c. of castor oil.

About half a century ago carbon tetrachloride was studied for its anesthetic value when administered by inhalation. It seems to act somewhat like chloroform. As the drug might act on the liver in a manner similar to the action of chloroform in delayed chloroform poisoning, experiments on dogs were undertaken. No macroscopic changes were noted in the liver after oral administration of carbon tetrachloride in doses up to 1.5 c.c. per kilogram of live weight, though the acute yellow necrosis due to chloroform is unmistakable in dogs after doses of 0.3 c.c., per kilogram.

An advantage of this drug would be the absence of discomfort and subjective effects as shown by a test the author made himself. Using the dose found effective in freeing dogs from hookworms, 3 c.c. of carbon tetrachloride were swallowed in hard capsules, three hours after a light breakfast. Seven minutes after taking the drug, there was an eructation of carbon tetrachloride, and, during the first half hour, there was a sensation of warmth, not sufficient to be called a burning sensation,

(3) Jour. Amer. Med. Ass'n., Nov. 19, 1921.

in the abdomen. This sensation passed away after a short time. There was no evidence of constipation, the drug apparently having a mild laxative effect. The production of headache, nausea, burning sensation in the stomach, etc., by such drugs as thymol and chenopodium, frequently makes it difficult to give a second treatment or to bring in new patients after the word has passed around that some have been made ill by the treatment.

The author also had the opportunity to make some toxicity tests of carbon tetrachloride on monkeys. From these the apparent safety of carbon tetrachloride is likewise indicated. Carbon tetrachloride is much cheaper than chenopodium or thymol, and can be purchased almost anywhere at any time. It does not depress unstriated musculature or lessen peristalsis. An immense saving might be effected by the omission of a purgative in carrying on hookworm campaigns involving millions of people. It may be said in passing that it is apparently of no value for removing tapeworms.

RESTORATIVE THERAPY

PROTECTANTS.

Calamine in Treatment of Hemorrhoids. J. C. Lyth⁴ advises that after the bowel movement, which should take place at night, and after gentle sponging with tepid water, calamine powder be applied freely and thickly on a sanitary wool (absorbent cotton) and gauze pad in contact with the piles.

Paraffin Film as Antipruritic. A. Kissmeyer⁵ calls attention to the use of paraffin films in dermatology not only for the healing of leg ulcer, but also and most especially in eczema, in neurodermatitis, prurigo and Roentgen-ray burns. While it did not always secure healing it never failed promptly to lessen the itching. The film he finds most valuable is composed of benzoin 1, caoutchouc 5, paraffin (melting point 52°C.) 100 parts.

Paraffin Film Treatment of Burns. Harry Cohen⁶ considers paraffin treatment especially indicated in ex-

(4) Brit. Med. Jour., Feb. 19, 1921.

(5) Ugeskrift f. Laeger, April 7, 1921.

(6) New York Med. Jour., Aug. 17, 1921.

tensive burns. It is superior to other well-sponsored forms of treatment, which the author reviews and criticizes as follows:

Carron oil almost always infects the wound. Wet dressings, *e. g.*, of aluminum acetate are difficult to keep wet; and, if drying is permitted, adhesions form between the gauze and tissue; the gauze becomes enmeshed in the burned surfaces and granulations; and its removal is a very painful, barbarous procedure. The continuous bath treatment has no special advantages over other methods, and is difficult to carry out. Picric acid in 1 per cent. solution as a wet dressing has many exponents and undoubtedly possesses excellent healing qualities; but it stains everything yellow, and in extensive burns may cause toxic symptoms due to absorption of the picric acid. There are countless numbers of ointments in use, boric acid being the one most frequently employed. Others are salicylic acid, resorcin, dermatol, and zinc oxide. Although each has some good qualities, they are relatively expensive, require considerable gauze, are not easily handled, stick to the tissues, and do not prevent ugly scars and contractures from forming. The open-air treatment consists in placing the patient in bed and leaving the burned parts exposed to the air, the other parts of the body being well covered. In warm weather cheese cloth or mosquito netting is placed over the bed to keep flies from the wound. The odor and appearance of the wound are two objectionable features, as is also the tendency of the patient to pick off the scabs, and the fact that disfiguring scar formation frequently follows.

Treating burn cases with adhesive plaster strips about one inch wide and slightly overlapping each other, as well as using sterile rubber tissue or silver foil strips has also the objection that unsightly scar formation very frequently follows.

With the paraffin treatment, frightful disfigurement and loss of function are practically eliminated. The paraffin does not cure, it simply acts in a mechanical way allowing Nature to heal under conditions favorable to repair. It excludes the air, maintains a constant temperature, and forms a protective dressing. It serves as a superstructure or scaffolding to new epithelium which

rapidly regenerates, and as a poultice and cast. A secretion soon forms under the dressing which makes it easy to remove without pain, or bleeding or destroying the new regenerated epithelium, thereby facilitating the healing without apparent contracting cicatrices and without causing functional disability.

If the paraffin is applied with an atomizer there is no need of controlling the temperature of the wax as it is impossible to burn the patient. The burn must be dressed daily, when a considerable discharge of sero-pus will be found under the paraffin, loosening and lifting it up and making its removal easy and painless. Where pus is too profuse or where absorption symptoms occur (fever, redness, and swelling) the paraffin treatment is discontinued for a day or two and the Carrel-Dakin solution applied. In extensive burns, early grafting, usually in about three weeks is advisable.

Cohen gives a comparison of three cases, burned at the same time and to about the same extent, to each of which different treatments were applied. A girl whose entire back from neck to gluteal folds, plus two arms was burned, received a modified open air treatment. Duration of stay in the hospital was seven and one-half months. Length of time of subsequent dressing seven and one-half months, giving a total duration of treatment of fifteen months. There was considerable scarring and keloid formation.

A boy, similarly burned, was treated with ointment adhesive strips for seven months and is still being dressed, fifteen months after the accident. Ugly scarring is evident.

A woman whose entire back from neck to gluteal folds, plus one arm, was burned also to the third degree, treated with "ambrine," stayed in the hospital three months and one week. She was subsequently dressed, for one month, which made a total duration of four months, one week. There was slight scarring.

A comparison of these three cases shows in favor of the paraffin dressing: (1) enormous time saving; (2) dressings painless and comfortable; (3) minimum scarring.

F. P. Horan⁵ finds the most satisfactory local treatment of burns to be the use of Dichloramine-T, followed by a paraffin or other fatty film. The entire burned surface of the patient is sprayed with a 2 per cent. solution of dichloramine-T dissolved in chlorocane. There may be a slight tingling sensation for a couple of minutes after which the pain will almost entirely disappear. In some cases, following the dichloramine-T application, he sprayed the surface with parresine and covered the entire area with large compresses. In many of the cases he has not used the parresine at all; but instead, where extensive destruction of tissue has taken place, he simply applied compresses soaked in dichloramine-T directly to the part involved. The dressings were changed daily. The advantage of dichloramine-T is that it is an antiseptic and that it keeps its antiseptic properties for twenty-four hours and has an oily base which permits the dressings to be changed with perfect comfort to the patient. When, after several dressings with dichloramine-T, no infection has developed and granulations are beginning to appear, Horan covers the area which has been sprayed with dichloramine-T with vaseline compresses that have been aseptically prepared. The vaseline compresses are made with a mixture of 91 parts vaseline, 6 parts paraffin, 3 parts resin.

ASTRINGENTS, STYPTICS, HEMOSTATICS

Influence of Reaction on the Precipitation of Proteins by Tannin. T. Sollmann⁶ shows by means of test-tube experiments, in which the hydrogen-ion concentration varied from pH-1 to 10, that the precipitation of protein by tannin depends on the hydrogen-ion concentration of the medium. With concentrations of tannin such as would be used for astringent effects (from 0.1 to 0.5 per cent.) precipitation is maximal between pH = 2 to 5; with greater acidity or alkalinity, the precipitation becomes smaller. With alkalinity greater than pH = 8 or 8.3 there is no precipitation and therefore no astringency. The limits are somewhat more

(5) Illinois Med. Jour., August, 1921.

(6) Jour. Pharm. and Exper. Therap., August, 1920.

narrow for dilute than for concentrated solutions of tannin. The precipitation limits are essentially the same for native proteins (serum and albumin) and for "Witte peptone." These data suggest the following as to astringency by tannic acid in the alimentary tract:

"The resting empty stomach would permit precipitation of the mucosa, and therefore astringency or irritation of the stomach. The tannin would thus be bound probably completely and prevented from acting on the intestine.

"When taken with food there would be some astringent action, but the precipitation would involve mainly the food proteins. These precipitates would also adsorb some of the tannin. The precipitation would at first increase with the acidity; but at the maximum acidity, a part would be redissolved.

"The chyme when it reached the duodenum, would contain tannin in the form of protein precipitates, adsorbed tannin, and redissolved tannin.

"In the duodenum, the conditions would be favorable to further precipitation, and therefore to astringent action.

"The reaction of the entire small intestines would permit precipitation, if any tannin were available. However, the reaction becomes progressively less favorable from the duodenum downward. Consequently, no further precipitation could occur after the duodenum or jejunum, except by the liberation of bound tannin. Such liberation occurs to some extent by the ultimate cleavage of the protein by which the tannin had been bound or adsorbed. However, this can extend only so far in the intestine as protein-cleavage extends; for the liberated tannin would be immediately bound by the intestinal mucosa.

"It is, therefore, impossible that the astringent action should extend to the large intestines, unless peristalsis or protein cleavage are very abnormal, as for instance in cholera.

"Solutions of krameria or catechu would behave like tannin, and it is difficult to see how they could have much advantage. The crude drugs or solid extracts

might possibly be superior, namely, if they dissolve only slowly in the intestines.”

Astringent Collyrium. Richter⁷ recommends in severe acute conjunctivitis, the following prescription which has given relief in cases in which other astringents failed :

| | | |
|--|-----------------------|---------|
| R | Sodium borate | 2.0 |
| | Tannic acid | 0.3-0.5 |
| | Distilled water | 50.00 |
| M. Label. A few drops in eyes morning and evening. | | |

Permanganate of Potassium as a Styptic for Serous Surfaces. In cases of hemorrhages from superficial wounds of the serosa after separation of adhesions J. Dsirne⁸ has used potassium permanganate crystals with best results. One or more crystals of the salt picked up with a pair of dissection forceps and applied to the bleeding points instantly coagulates the blood, forming a black, dry, aseptic scab. After some seconds the scab is cautiously removed with fine blunt forceps; and on the wounded surface of the serosa there remain only black spots. If the bleeding surface is large, a pinch of permanganate crystals is folded in a piece of lint and applied to the wound for a few seconds. The author has employed this method for nearly twenty years without any complications.

L. Buckley⁹ has tried the drug on various bleeding surfaces, uncontrollable by other styptics, with entire success. Thus in stubborn bleeding after tooth extraction the application of a little powdered potassium permanganate into the bleeding cavity and pressure upon it with a piece of absorbent cotton soon stops the bleeding. In cuts of the scalp (not too extensive cuts of course) a sprinkle of the powdered drug over and into the cut surfaces promptly stops the bleeding, protects the open wound from the outside infection, and speeds up the healing process. So much does he rely on the styptic and antiseptic powers of this drug that in scalp cuts of medium size after the powdered drug is applied to the

(7) Deutsch. med. Wochenschr., 1921, p. 717.

(8) Lancet, June 25, 1921.

(9) Critic and Guide, October, 1921.

surfaces, no further protection by bandaging is practiced. He has never noticed any infection developing in such cases when so treated. He uses the powdered drug, not the crystals, as Dr. Dsirne advises, for the following reasons:

1. The powder having no sharp edges, as the crystals have, its application to the bleeding points or surfaces is less painful.

2. The powder, more completely than the crystals, covers the entire bleeding surfaces and more promptly stops the oozing of the blood.

3. It takes less time to sprinkle a little powder over a bleeding surface than to touch up every bleeding point with a crystal or crystals as Dr. Dsirne does.

4. Occasionally it is necessary to press the drug gently but firmly into the bleeding surfaces; this can be done with the powdered drug but not with the crystals.

Intramuscular Injection of Calcium Chloride as Hemostatic. W. R. Grove, and H. W. C. Vines,¹ in view of the fact that calcium administration by mouth has no effect upon blood calcium, advocate intramuscular injection of calcium chloride by the following technique: One grain of calcium chloride is dissolved in about 100 minims of water and injected deeply into the gluteal muscles; it must not be injected subcutaneously or sloughing of the skin will be caused. If a solution of the salt is made up to a concentration of 1 in 4, 4 minims then contain 1 grain. This solution has been kept for weeks, and in this strength apparently remains sterile indefinitely. The 4 minims are diluted to 100 minims with boiled water, and in some hundred or more injections nothing abnormal has developed at the site of injection. The calcium value in the blood is found to rise slowly, as the result of such injections, to a maximum in six hours; and then to remain practically constant for at least twenty-four hours. It has been found perfectly safe to give a second injection at the end of twenty-four hours; and, if necessary, a third one twenty-four hours later. In anticipating hemorrhage at or after operation, an injection not more than two hours before, or even at the time of operation, would seem indicated.

(1) Brit. Med. Jour., July 9, 1921.

Hemostatic Action of Ethylenediamines. Nonnenbruch, and W. Szyszka² noted that the blood coagulated with extraordinary rapidity after ephyllin injections. Further studies showed that, like ephyllin, which is theophyllin-ethylenediamine other ethylenediamines such as piperazine (diethylenediamine) or ethylenediamine acetate, increase the coagulability of the blood, while caffeine and theophyllin do not possess this action to a marked degree. The coagulation is increased by over 50 per cent., probably due to increase in fibrin ferment. In several cases of hemoptysis intravenous injection of 0.48 gm. ephyllin caused prompt cessation of the bleeding.

Effect of Hemostatic Serum (Hemoplastin, P. D. & Co.). H. C. Hamilton³ dissents from the conclusion of Hanzlik and Weidenthal,⁴ that the serum products including hemostatic serum did not accelerate clotting, and that, therefore, these are inert as thromboplastic agents. The chief objection to the method employed by Hamilton, the repeated withdrawal of relatively large quantities of blood, was that bleeding progressively increases the coagulability of the blood, and that the results of such bleeding tests are so irregular as to be of no scientific value. Hamilton, however, establishes certain conditions which he considers prerequisite for the test as he employs it, and by means of which, irregularities are to a great extent eliminated. In this paper, he publishes a series of observations upon horses in which the amount of blood withdrawn was certainly too small in relation to the total amount of blood in the animal to have any appreciable effect upon the coagulation time of the blood. His protocols show a decided acceleration of clotting following the injection of hemostatic serum.

ANTITHROMBIC THERAPY

Sodium Citrate Treatment of Thrombo-Angiitis Obliterans. William A. Street⁵ obtained fairly satisfactory results in this ordinarily intractable condition by

(2) *Deutsch. Arch. f. klin. Med.*, 1920, p. 174.

(3) *Jour. Lab. and Clin. Med.*, April, 1921.

(4) *Abstracted in Practical Medicine Series*, 1920, Vol. VI, p. 106.

(5) *Jour. Amer. Med. Ass'n.*, Feb. 12, 1921.

a treatment which consisted of posture and the application of heat plus sodium citrate injections. During the first month, the patient was kept in bed with the legs in an electric light hot air atmosphere of 110° F. An intravenous injection of 250 c.c. of 2 per cent sodium citrate solution was made every second day, During the second month the injections were made every third or fourth day; the legs were massaged and allowed to hang down for a short time each day. Even walking was permitted if the condition of the patient indicated it. At the end of a year, the patient received one injection every two weeks and the walking was increased as there were indications of the establishment of collateral circulation.

Potassium iodide, in doses of 10 drops three times a day, was given during the whole course of treatment. The injections were made in the veins of the arm through a curved slip point needle by the usual skin puncture method.

Six cases are reported. The time since the treatment varies in duration from one month to one and one-half years. The effects were: (1) relief of the pain after second injection, (2) the checking of gangrene, (3) the healing of indolent ulcer, (4) the slow establishment of collateral circulation and, in some cases, the return of the pulse in the anterior and posterior tibial arteries. Some of the patients have returned to active work.

ALKALIES

Alkali in Acidemia of Chronic Nephritis. B. S. Cornell⁶ reports that, after, say, four doses (1.3 gm. each) of sodium bicarbonate by the mouth, the most severe nephritic dyspnea subsides, and usually disappears altogether, providing the heart had no part in causing the respiratory distress. This observation is useful in the treatment of dyspnea. The physician will frequently meet a nephritic whose distressing dyspnea fails to respond to digitalis; he has no cyanosis or cardiac enlargement or signs of cardiac decompensation. To this patient sodium bicarbonate in sufficient doses gives prompt relief. There is no contraindication to its use.

(6) Jour. Amer. Med. Ass'n., March 12, 1921.

The only caution, perhaps, should be not to render the urine alkaline for too long a period, thereby facilitating phosphatic deposits.

Alkali in Impending Diabetic Coma. W. E. Cary's⁷ experience with two cases reported in detail indicates that the precoma in diabetics with low reserve of alkali, the symptoms of acid intoxication, can be promptly eliminated by the immediate recourse to alkali—preferably by mouth but, if absolutely necessary, by other routes in addition—when, as in the cases described, no other procedure alone will avert death. He emphasizes the importance of getting from 25 to 50 gm. of the alkali into the body within the first two hours. The reaction of the urine should be carefully observed, and frequent tests of the urine or blood made to prevent over-alkalization. In severe cases, the immediate danger of coma passes when the reserve is brought to 30 and conservatism in going above 40 may possibly be wise, although Cary has never seen any harmful results that could be attributed to the use of alkali in these cases.

Dose and Methods of Administration: Cary calculates that a plasma carbon dioxide of 40 would imply the necessity of giving the patient 85 gm. of soda as quickly as permissible. Setting six hours as the time within which the dose should be given, and four hours, if possible, three routes of administration are available: (1) mouth or stomach tube; (2) bowel, or (3) vein. These are discussed in the reverse order of importance in these cases. Intravenous administration is to be considered only in cases in which administration by other routes proves insufficient. As is well known, a sodium bicarbonate solution can not be boiled without partial conversion of the bicarbonate to the carbonate; and, for the preparation of a sterile solution, special precautions are necessary. One may follow the plan used by Sellards, or the powdered bicarbonate may be sterilized in sealed tubes and then added to the sterile water, making a 4 to 5 per cent. solution. Unless the material has been prepared beforehand, its preparation is liable to cause a loss of valuable time; and further delay may be caused by assembling the paraphernalia necessary for the intravenous injections itself. When all is ready, 400 c.c.

(7) Jour. Amer. Med. Ass'n., May 21, 1921.

of this solution every hour is about as much as one should attempt to give.

By the bowel, one may employ a 3 per cent. solution and succeed in giving it at the rate of 300 c.c. an hour by the drip method. Giving 9 gm. of the soda every hour by this route for three or more hours, is as much as can be anticipated.

Administration by mouth is the most satisfactory method in diabetic cases. Although some diabetic patients with high acid intoxication vomit during the early stages, they will usually retain sodium bicarbonate surprisingly well. They differ in this respect from many cases of acidosis with nephritis. Cary has usually found it possible to give as much as 20 gm. of sodium bicarbonate by mouth as first choice in every case. In comatose cases, the alkali may be given if necessary through the stomach tube. However, a case in which the patient has sunk completely into coma is usually hopeless; and unless a patient is actually comatose, it will commonly be found possible to nurse the alkali solution along, a spoonful at a time, if the effort is faithfully made. If the rate of administration by mouth falls behind 15 gm. an hour for one or two hours, accessory methods should be called on early to make up this deficiency; first, the rectal drip, and then the intravenous injection, if the latter is unavoidable. The introduction of massive doses of soda necessarily increases the osmotic concentration of the body as a whole. Increased thirst is therefore to be expected, and great care should be taken to provide for an adequate intake of water along with the soda. For the purpose of supplying water, the bowel may well be used, thus reducing the volume of liquid given by the stomach. To this end the oral administration of the bicarbonate may be supplemented by the rectal administration of physiologic sodium chloride solution at the rate of from 400 to 500 c.c. an hour. [Tap water would be better for this purpose.—Ed.]

ACIDS

Pepsin and H-Ions. H. T. Graber⁸ corroborates the demonstration by Sørensen that the action of pepsin is not dependent upon the titrable acidity but rather upon

(8) Jour. Amer. Pharm. Ass'n., June, 1921.

the H-ion concentration. It is universally recognized that the pepsin digest, when egg white is used as the proteid under digestion, takes place best in a medium of 0.3 per cent. HCl and at a temperature of 52° C. If the peptic activity were dependent on the titrable acidity alone, it would be only necessary to adjust other acids, both organic and mineral, to this same 0.3 per cent. strength to obtain the same activity, assuming that the acid employed does not directly inhibit peptic digestion. Experiment proved that this is not the case when various acids are used. This is due to a difference in the concentration of "H" ions. When H-ion concentration was adjusted to be equal to that of 0.3 per cent HCl, phosphoric acid of 49.00 titrable acidity digested equally as well as the hydrochloric acid with a titrable acidity of 0.3 per cent. It was also found that phosphoric acid brought to the same H-ion concentration as 0.3 per cent. HCl at 52° C. before adding egg white is just as efficient as the HCl in activating peptic digestion. On the other hand, acetic and citric acids brought to the proper H-ion concentration at 52° C. before adding egg white are not efficient activators of pepsin digestion after the egg white is added. This is perhaps due to the strong depressant action of the egg white which acts as a buffer toward these weakly dissociated acids.

Dangers of Hydrochloric Acid Administration. J. C. McClure, and H. A. Ellis⁹ conclude that the opinion generally held that dilute hydrochloric acid is a more or less harmless drug of tonic properties is erroneous. They have found cases of acid sensitiveness showing such an intolerance of acid that even a dose of 5 minims thrice daily was keenly resented. This sensitiveness, sometimes occurring in persons who are perfectly healthy, is manifested in two ways: (1) by nausea and vomiting, following rapidly on a dose of the acid—apparently a local intolerance; and (2) by the gradual development of circulatory difficulties accompanied by a rise in blood-pressure—a condition probably of renal origin. It is especially individuals whose renal function is crippled who are curiously "acid sensitive"; and in these very small doses of dilute hydrochloric acid will

(9) *Lancet*, Aug. 6, 1921.

raise the blood-pressure and induce unpleasant symptoms.

Hence, when acid is being administered, the blood-pressure should always be estimated from time to time, and the urine be tested for its acid and ammonia relations. In cases in which an early condition of renal insufficiency is suspected, the "rest urine" should be compared with the "alkaline tide urine" in respect of the relative acidity. When this general acid sensitiveness occurs accompanied by a rise in blood-pressure, acid administration and acid feeding are contraindicated. During treatment with acid, a rise in the blood-pressure may be followed by a more or less similar fall, which is not easily reversible. This occurs because the acidosis may be transferred to the tissues, the acidemia thus being changed into a histo-acidosis, and this causes a fall in the blood-pressure. If a histo-acidosis be established, it is not easy to raise the blood-pressure again, because of the difficulty either of raising the acid content of the blood above that of the tissues or of reducing the acidity of the tissues below that of the blood, the fluid pressure thus persisting toward the tissues, while the balance is against the blood. In such cases, edema may occur.

ALTERATIVES

Phosphorus in Rickets. In a previous report D. B. Phemister¹ showed in Roentgen-ray studies the influence of phosphorus on the growth of normal bones and the bones in the growth disturbances of osteogenesis imperfecta and dyschondroplasia. A dense shadow formed at the growing ends of the shafts, which gradually increased in thickness as long as the phosphorus was given. Miller and Phemister repeated Wegner's classical experiments on dogs and partially confirmed his findings.

This led Phemister, E. M. Miller and B. Bonar² to undertake observations on the bones in rickets to study the influence of phosphorus and cod-liver oil and of phosphorus alone. Four cases were studied. Two on phosphorus and cod-liver oil, and two on phosphorus alone.

(1) Practical Medicine Series, 1918, Vol. VI, p. 97.

(2) Jour. Amer. Med. Ass'n. March 28, 1921

It was found that the end-results produced by phosphorus, and the combination of phosphorus and cod-liver oil were quite similar. The rarified areas of the rachitic bones acquired an approximately normal density in both instances.

That cod-liver oil alone may produce such changes has been shown by Howland and Park (1920), who have made extensive studies of its effect on rickets. Prompt healing was obtained with the formation of a double line in the juxta-epiphyseal region of the shaft and ossification of other rarified areas of the bones.

The method of action is little understood. In the case of cod-liver oil the result might be attributed to the presence of the fat-soluble vitamin A; but this could not be the explanation for the action of phosphorus. While there is a trace of phosphorus in cod-liver oil in organic combination, it is improbable that it is present in sufficient quantity to exert any influence. Clearly phosphorus, and also cod-liver oil, in some way restore the power of normal ossification, which in rickets is temporarily lost.

Calcium in Pulmonary Tuberculosis. E. E. Prest³ has been giving calcium lactate (1 gm. in powder form at bed time during alternate weeks) to a majority of the ninety-four patients in the Ayrshire Sanatorium and is convinced of the benefit accruing. The female loses a great deal of calcium with the menstrual blood; hence in cases of excessive ovarian activity calcium may become deficient. In many girls and young women, and in some women at the menopause who are found to be also suffering from pulmonary tuberculosis, one of the distressing symptoms is menorrhagia; this condition can almost invariably be benefited by the administration of calcium. Calcium largely ceases to be excreted during pregnancy, the retained calcium being used up by the growing fetus; during lactation calcium is largely secreted in the milk, and this probably is the chief reason why lactation has such a prejudicial effect on tuberculous women. The high content of calcium in milk may be one of the reasons for milk holding such an important position in the dietary of the tuberculous; and therefore

(3) Brit. Med. Jour., March 19, 1921.

when milk is difficult to obtain it might be well to give children calcium. The reproductive organs seem largely responsible for calcium waste, and even in males sexual excesses are accompanied with calcium loss. Prest has found calcium useful in treating young adult males, and it would probably be useful in the treatment of neurasthenia.

The effects observed during the administration are: Fall in temperature, cessation of night sweats (rare in sanatorium), increase in energy, cessation of menorrhagia, retrogressive changes in the lesion, and benefit to the anemic conditions.

ORGANOTHERAPY

Epinephrine in Addison's Disease. A. L. Muirhead⁴ reports his experience with epinephrine in his own case of Addison's disease. Hypodermic injections of one-half to 1 ampule containing 1 c.c. of a 1:10,000 solution, given twice daily produced improvement almost at once. The earliest results were relief of the feeling of tension in the abdomen and an increased food tolerance. Soon an increase in strength and endurance was noted. An attempt was made to use a solution of epinephrine in dilute mucilage of acacia for the purpose of delaying absorption and prolonging the epinephrine action. A comparison of the blood-pressure results after the administration of $\frac{1}{200}$ of a grain of epinephrine in sterile salt solution and the same amount in acacia solution, hypodermically, is shown in Figure 9.

Epinephrine solution by rectum was tried also, and the sphygmomanometer revealed positive pressure results. Figure 10 shows the amount and duration of increased pressure produced by rectal injection of 2 c.c. of a 1:1,000 solution of epinephrine diluted with physiologic sodium chloride solution. This method of medication was used twice daily for several months. Muirhead also used rectal injections of dried whole suprarenal gland, 10 grains dissolved in physiologic sodium chloride solution, but the pressure results were less marked and not definitely measurable. Of late, ampules of the

(4) Jour. Amer. Med. Ass'n., March 5, 1921.

1:1,000 solution have been used and the epinephrine tolerance has been found to be only 0.2 c.c. Larger doses cause uneasiness, trembling of the extremities, a sense of impending chill and a feeling of tension in the region of the removed kidney.

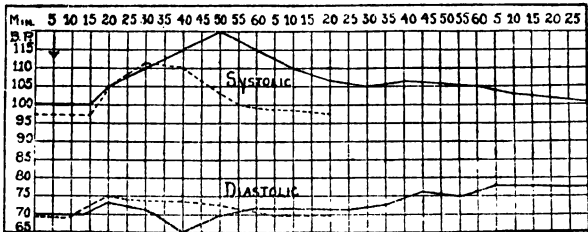


Fig. 9. Comparison of the effects on the blood-pressure of $\frac{1}{200}$ grain of epinephrine when administered hypodermically in physiologic salt solution (broken line) and when given in acacia muclage (solid line). Arrow indicates time at which epinephrine was administered.

At the present, the blood-pressure level is about as it was at the onset. The last reading was 92 systolic, and 64, diastolic. The marked improvement observed in spite

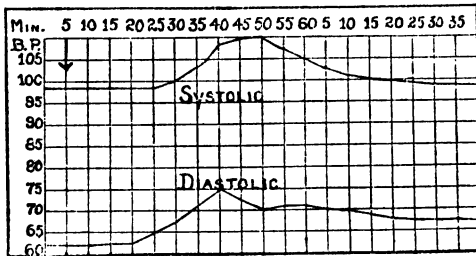


Fig. 10. Effects on blood-pressure of 2 c.c. of epinephrine solution administered by rectum. Arrow indicates time at which epinephrine was administered.

of the low pressure level would indicate a gradual adaptation of the organism to the low pressure level. The artificial supply of epinephrine no doubt aids body function, as a brief withdrawal recently was followed by some recurrence of gastro-intestinal symptoms.

Rectal and Colonic Injections of Epinephrine. H. G. Barbour, and F. H. Rapoport⁵ found by experiments that in rabbits epinephrine is absorbed both from the rectum and from the colon. Injected into the rectum, epinephrine causes a greater rise in blood-pressure than when injected into the colon. When epinephrine is injected into the colon, it causes a greater degree of glycosuria and diuresis than when injected into the rectum. The reason for this lies in the anatomic fact that absorption from the terminal portion of the mammalian intestine takes place by way of the middle and inferior hemorrhoidal veins directly into a branch of the vena cava. The colon, on the other hand, is drained by the portal system. Before the general circulation is reached, a barrier is interposed by the liver and its capillaries. The two extremes of the alimentary canal present its only absorption areas where such protection is not afforded.

[This probably also accounts for the promptness and efficiency of oral (sublingual) administration of drugs as contrasted with peroral (more commonly but less properly called oral) administration. [Practical Medicine Series 1917, Vol. VIII, p. 18.—Ed.]

Binet (1917), characterized epinephrine as "innocuous by stomach but very toxic by rectum."

Epinephrine in Bronchial Asthma. H. L. Alexander and R. Paddock⁶ argue that bronchial asthma is due to vagotonia, basing this assertion on the fact that in asthmatics there is an increased sensitiveness to pilocarpine and epinephrine. A small dose of pilocarpine which has no effect on a normal individual may bring on a typical asthmatic attack, though a dose large enough will bring on a typical asthmatic attack in the normal individual. The same holds true for epinephrine. Minute doses which do not have any effect on the blood-pressure of the normal, easily relieve asthmatic attacks.

Hence, the authors advocate the use of small doses of epinephrine: 0.25 c.c. of 1 to 1,000 epinephrine, a much smaller dose than is usually employed, as of greater value.

(5) Jour. Amer. Med. Ass'n., Feb. 19, 1921.

(6) Archiv. Int. Med., February, 1921.

Negative pilocarpine reactions do not necessarily rule out vagotonia; other signs and associated conditions must be looked for. These include eosinophilia, dermatographism, bradycardia, low blood-pressure, pulsus irregularis respiratorius, and the presence of status lymphaticus.

Duration of Constriction of Blood-Vessels by Epinephrine. S. J. Meltzer and John Auer⁷ studied, by ocular observation, the duration of vascular constriction produced by adrenalin (Parke Davis & Co.) injected subcutaneously into one ear of a rabbit. They found the constriction to last in general from 180-480 min. (3-6 hrs.) as against a maximum of 7 min. duration of blood-pressure rise after intravenous injection. The duration of the constriction is longer in general with larger doses and with proximity of the injection to the central artery of the ear. After the vasoconstriction passes off, the vessels of the ear show a tendency to dilatation. A subcutaneous injection of adrenalin in one ear, which causes a constriction of the vessels of that ear, seems often to cause at about the same time a dilatation of the vessels in the other ear; the dilatation is not of long duration.

Epinephrine Polycythemia. This subject has been studied by Paul D. Lamson,⁸ who has investigated the cause of the sudden marked increase in the number of red blood corpuscles per unit volume of blood which occurs when epinephrine is given intravenously, but which fails to take place when the liver is removed from the circulation. Lamson ascribes this to an obstruction in the venous outflow from the liver, causing a swelling of the liver and temporary retention of fluid in the liver lymphatics. The physiologic polycythemias of exercise, asphyxia, increased blood-pressure and emotional disturbances might all be of the epinephrine type. The author presents evidence that normally there is no reservoir of red corpuscles in the body, sufficient to increase the red blood count appreciably and that all sudden polycythemias in which there has not been sufficient time for red cell production are due to loss of fluid

(7) Jour. Pharm. and Exper. Ther., April, 1921.

(8) Ibid., September, 1920.

from the circulation. Besides retention of fluid in the liver, as has been shown to occur in the epinephrine polycythemias, Lamson recognizes two other types—namely: the one occurring in endothelial poisoning, as the injection of histamine in which case fluid is lost into the various tissues directly; secondly, loss of fluid into passages of the body as in the case of diarrhea of cholera, and the loss of fluid into the bronchi in gas poisoning.

Pituitary Extract. Its Dangers. M. P. Rucker and C. C. Haskell¹ arrive at the conclusion that the use of pituitary extract is accompanied by danger to the mother and to the child. The injurious action on the mother is manifested by an increase in the frequency of perineal lacerations and the occasional occurrence of uterine rupture, *in cases in which all the indications for the use of the extract are present.* The dangers to the child consist in the greater tendency toward the production of asphyxia and toward the occurrence of intracranial hemorrhage.

The authors have been able to secure graphic evidence of tetanizing action on the human uterus *in situ* by introducing a Voorhees bag into the cervical canal and connecting its interior with a mercury manometer.

The uterine contractions were recorded on the smoked surface of a kymograph. Even doses of pituitary extract as small as 2 minims cause a persistent increase in the tone of the uterus. As is the case with the uteri of lower animals, there are similar contractions superimposed on the tonic increase in pressure, but the base line does not return to its original level for some time, as long as twenty-eight minutes after one dose of 2 minims. After the injection of 0.5 c.c., the increased tonus persisted for thirty-five minutes. In two tracings, the level of this new base line was above that of the height of the individual contractions occurring before the administration of the drug; in other words, there was a constantly maintained intra-uterine pressure decidedly higher than that existing at *the height of the individual contractions* before the drug was injected. They quote the following statistics from The Memorial Hospital of Richmond, which speak for themselves.

(1) Jour. Amer. Med. Ass'n., May 21, 1921.

COMPARATIVE RESULTS WITH AND WITHOUT
PITUITARY EXTRACT

| | Number of Cases | Infant Deaths | | Free from Lacerations | | Lacerations | | | |
|--------------------------------|-----------------------|------------------|-----|--------------------------|------|-------------|------|-----------|------|
| | | No. | % | No. | % | 1st Degree | | 2d Degree | |
| | | | | | | No. | % | No. | % |
| With pituitary extract..... | 34 | 3 | 8.8 | 11 | 32.3 | 12 | 35.3 | 11 | 32.3 |
| Without pituitary extract..... | 59 | 2 | 3.4 | 36 | 61 | 16 | 27.1 | 7 | 11.8 |

An examination of necropsy records of eleven still-born infants showed that subdural hemorrhage occurred in none of nine cases in which the mother had not received pituitary extract, while subdural hemorrhage occurred in two cases in which pituitary extract had been given to the mother; once in the small dose of 0.5 c.c. If the possibility of intracranial hemorrhage is increased by the use of pituitary extract, the death of the child is not the only catastrophe to be feared. Diffuse nervous lesions due to cerebral hemorrhage result in terrible afflictions. Such cases are reported in literature. Hence the authors believe there is always the possibility of harm resulting even from the so-called "safe" doses, a danger so real that it is scarcely justifiable to risk it for the sake of a few added hours of rest or those left free to be devoted to other tasks by the obstetrician.

Pituitary Extract and Histamine in Diabetes Insipidus. R. B. Gibson and F. T. Martin² report a case of diabetes insipidus in which the administration of 1 c.c. of the obstetrical preparation of pituitary extract subcutaneously temporarily increased the concentration and reduced the volume of the urine. Histamine, which is thought to be the active principle of the posterior lobe of the hypophysis, gave similar results; but was less effective.

Therapeutic Uses of Anterior Pituitary Gland. T. B. Scott, and F. W. Broderick⁴ direct attention to pituitrin, the active principle of the anterior lobe, which we must differentiate from pituitrin, the active principle of the posterior lobe. The work of Goetsch and Robertson has shown conclusively that the development

(2) *Archiv. Int. Med.*, March, 1920.

(4) *Practitioner*, October, 1921.

and proper conservation of the genital functions can not be secured without the active assistance of anterior lobe secretion. The application of this knowledge should prove very valuable.

Much has been done by thyroid treatment, but still more would be accomplished if we realized that thyroid and anterior pituitary deficiency generally exist together. The thyroid perhaps tells more on the brain and nervous development and the pituitary on the osseous and the sexual, but no fast line can be drawn between the two influences. We see often the slow developing, dull adenoid type improve rapidly under thyroid, so far as intellect is concerned, but the body and limb growth falters. Here the combination does excellently well. In girls, especially, the intellectual life may be active and even brilliant, but the uterine and ovarian development are almost standing still, unobserved and untreated; these girls grow up sex failures. Never advancing beyond rudimentary growth of uterus and ovaries, they swell the ranks of the disappointed, the sterile, and the nervous invalids. They often begin to menstruate at 13 or 14, and go on for a year perhaps; then comes irregularity or complete cessation. This state of things, when not due to manifest anemia, points almost conclusively to hypopituitarism, and can be helped wonderfully by anterior pituitary medication. It should be given in good doses for two to three years, or till healthy menstruation is well established. Under its influence the pelvic organs develop as Nature demands.

It is well known that children of both sexes, who have enuresis, often recover under thyroid, but there are failures also, and, in these, the combination of the two gland extracts will often succeed. Failures of normal skeletal growth and osseous development especially demand pitglandin. While the anterior pituitary secretion promotes growth and develops function in early life, in old age it maintains function and for a long time counteracts the tendency to degeneration of tissue. This and thyroid, together, are the conservators, natural, not artificial, of life and energy. After the age of 55 or 60, pitglandin failure is generally associated with thyroid failure. The symptoms are the well-known ones generally classed un-

der subthyroidism. These are, raised blood-pressure with its usual signs of cardiac strain and fatigue, shortness of breath, and easily-produced muscular fatigue. If the cerebral arteries are affected, there may be vertigo and tinnitus. In short, there are the symptoms of early arteriosclerosis: premature sexual and vesical weakness, which so often occur, point to pitglandin deficiency. In practice, it is found that combinations of the thyroid and pitglandin are most effective, the pitglandin balances effectually the depressing effects of the thyroid, but it should be given in full doses, from 2 to 6 grains of dried extract daily. Pituitrin should be avoided, for it tends to raise blood-pressure.

Pitglandin holds out much promise in senile epilepsy. The author reports three cases of epilepsy in men between 70 and 85, relieved by doses of 0.03 to 0.09 gm. of anterior pituitary twice daily. The mental condition of these three men has much improved and their temper also.

Bile in Obstinate Diarrhea. Acting on the hypothesis of biliary insufficiency, W. H. Lewis⁵ administered from 2 to 4 gm. of ox bile every twenty-four hours to his patients suffering from diarrhea with greyish offensive stools, not relieved by diet, fasting, or other medication. The result was immediate and marked. Bowel movements were reduced, resumed their normal color and consistency, and abdominal distress disappeared.

BLOOD TRANSFUSION

Blood Transfusion. As a result of their experience with 186 blood transfusions, I. S. Ravdin and E. Glenn⁶ consider it a specific in acute hemorrhage where the "limit of bleeding" has not been reached, in melena and in the hemorrhage of hemophilia. It is of definite value in primary pernicious anemia in hastening and prolonging remissions. It is indicated in cases of severe secondary anemia. After transfusion, operations on debilitated or anemic individuals may often be safely undertaken that otherwise would involve serious risk.

(5) South. Med. Jour., December, 1920.

(6) Amer. Jour. Med. Sci., May, 1921.

Transfusion in shock is not so efficacious as in cases of shock associated with hemorrhage. The authors have not been able to prove the value of transfusion in acute infections, but in chronic infections have had results justifying its use. Transfusion is of unproved value in acute leukemia. In aplastic anemia it is at the most a temporizing procedure. The difference, so far as reactions are concerned, between the citrate method and the Kimpton-Brown method was found to be practically *nil* and the simplicity of the former warrants its preference. They report the following proportion of reactions.

| None | Mild | Moderate | Severe | Death |
|------|------|----------|--------|-------|
| 127 | 45 | 9 | 3 | 2 |

In properly typed individuals there should be no mortality unless the transfusion is attempted as a heroic measure in a patient who otherwise has no chance at all. In an emergency where time means all and the typing sera are not obtainable, from 15 to 25 c.c. of the donor's blood may be injected into the recipient's circulation. If no symptoms occur within from three to five minutes, the transfusion may be continued.

Paul M. Krall⁷ presents the following *résumé* of the subject:

“The chief objections to inorganic salt solutions intravenously are: (1) The short time the salt solution remains in the circulation; and (2) The possible destructive effects upon the red blood cells, in at least certain types of cases. Solutions of acacia and gelatin are the most efficient artificial solutions for transfusion purposes, but discretion and care must be exercised, as dangerous reactions may be produced, with both gelatin and acacia. Transfusion of “vital red blood” is a life-saving measure, not only in hemorrhage where the restoration of blood volume is a vital issue, but in diseases in which the patient is in need of oxygen, nutritive elements, coagulins, antitoxins and bactericidal elements. Accurate typing of donors and donees before the blood transfusion is a recognized necessity. The main objection to the citrate method of blood transfusion is the occurrence of chills and fever; it is, however, admittedly

(7) Jour. Kan. Med. Soc., April, 1921.

the most convenient method. The direct method of blood transfusion is unquestionably the most efficient.”

Accidents Following Transfusion. B. M. Bernheim,⁸ while he admits the practical value and simplicity of transfusion of citrated blood, cites a number of unfortunate sequels. We must expect that in from 20 to 40 per cent. of all citrate transfusions a reaction of greater or less severity will occur. Hence there are at least two types of cases unsuited for citrated blood:

1. That in which there has been a hemorrhage of such intensity that the extreme limits of bleeding have been reached, and the patient is in such a state of shock that everything in the nature of additional shock must at all hazards be avoided.

2. Those states of anemia, either primary or secondary, in which the blood depletion has progressed to such limits that the patient is almost dead.

Whole blood transfusion, in which the percentage of reactions is hardly so much as 5 per cent., should be employed in these two great groups of cases. It is most unfortunate that the giving of whole blood necessitates a far higher degree of skill than does the giving of citrated blood. It requires great and constant practice and a real knowledge of surgical technique. There should be in every community at least one man competent to carry out the whole blood method; and every physician should learn to differentiate his cases, so that he may take advantage of this man's skill, and give to his charges that chance for life for which they consult him.

Transfusion of Citrated Blood. M. Hoffman and H. C. Habein⁹ offer the following apparatus which they hope will prove simple and satisfactory, especially to the physician who performs only an occasional transfusion: In the past, mainly two methods of injection of citrated blood have been used: (1) the gravity method, and (2) the three-way method with syringe. The objections to the gravity method are the lack of control of injection, the excessive length of tubing necessary to secure the proper amount of gravity, and the danger of contamina-

(8) Jour. Amer. Med. Ass'n., July 23, 1921.

(9) Jour. Amer. Med. Ass'n., Feb. 5, 1921.

tion from the outside air. The three-way method with syringe offers the objection that it is impossible to prevent contamination from the outside air, that it is clumsy, requires considerable assistance, and the blood must flow through a large amount of apparatus. Furthermore, the tubes must be long; and the small holes in the cock are very liable to become plugged. One of the greatest annoyances in this method is the tendency for the plunger of the syringe to stick. Forcing the blood through the small holes in the stop-cock undoubtedly has a tendency to break down the red cells, and this also may be a factor in the production of reactions.

The apparatus devised by the authors eliminates contamination from the outside air. The blood runs through a minimum length of rubber tubing, which is of large caliber. It is quickly collected into a flask containing a solution of sodium citrate. This is done by means of a partial vacuum within the bottle. Then by reversing the syringe the blood is injected into the patient in a uniform, steady, stream at any desired rate under positive pressure within the bottle. The sodium citrate solution is prepared from a chemically pure product in freshly distilled water. This is a 1.5 per cent. solution, and of this 20 c.c. are used for each 100 c.c. of blood which is to be transfused.

The details of the construction of the apparatus are well shown in the accompanying illustrations (Figs. 11 and 12). As can be seen, little material is required which the average practitioner does not already have in his equipment. The reversible pump was secured from a chest aspiration set. The manometer, which is desirable but not absolutely necessary, can be taken from any spring sphygmomanometer, and is of value only in determining pressure within the bottle. The remainder of the apparatus consists of a liter flask with a small neck and a wide, flat bottom. A filter flask such as is shown in the sketch is satisfactory, but any Erlenmeyer flask may be used. The small glass bulb inserted in the short tube C between the pump and the bottle is filled with sterile cotton. This prevents the injection of particles into the flask.

The amount of sodium citrate necessary is measured

into a sterile graduate, the tube B to the recipient is clamped, and the sodium citrate solution is drawn into the flask through the tube A by means of a partial vacuum produced within it. This indicates further

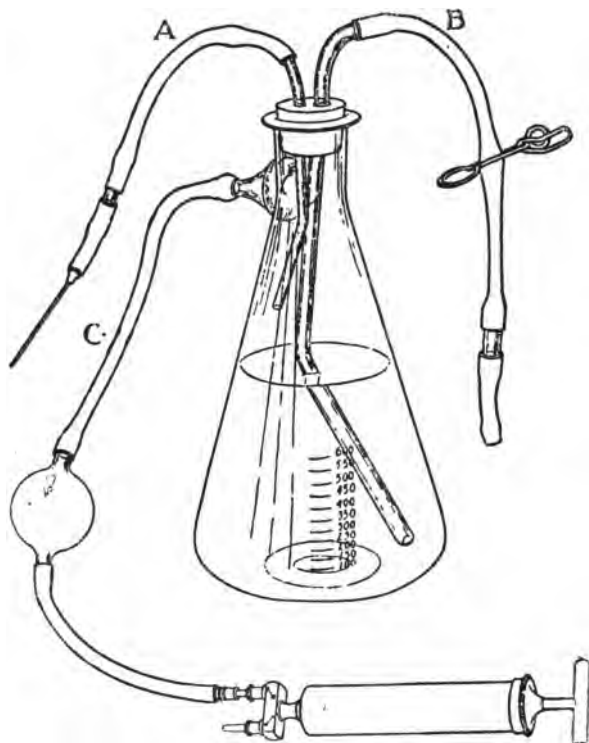


Fig. 11. Arrangement of apparatus for receiving blood from donor. Note the direction of the arrows on the pump and compare with the direction of arrows in Figure 12. This arrangement produces a partial vacuum within the bottle. A very small amount of vacuum is all that is necessary.

whether the pump is applied in the proper manner and will preclude any possibility of injecting air into the donor's vein. At the same time it rinses the receiving tube with sodium citrate solution, which helps prevent clotting.

To the end of tube A a large 16-gage needle is applied

(Fig. 11). As large a needle as possible should be used, but with this apparatus, on account of the suction, a much smaller one may be used than is necessary with other methods. The inside of all needles should be care-

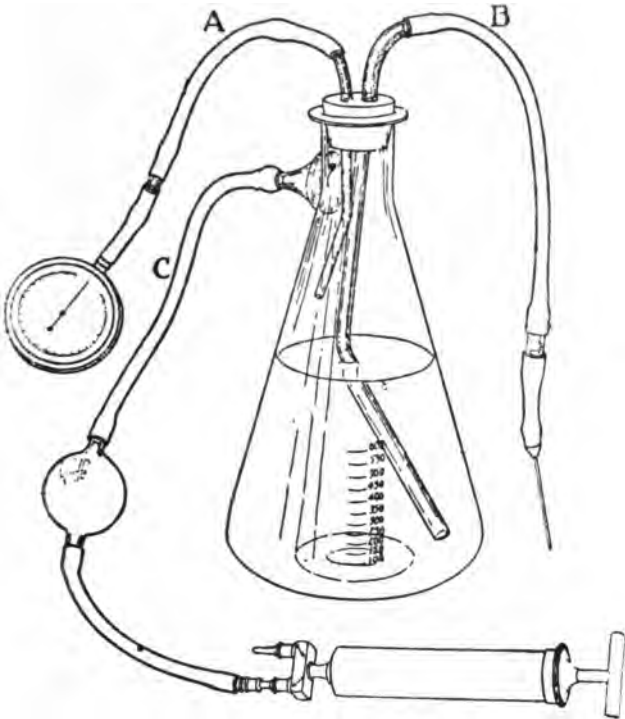


Fig. 12. Arrangement of apparatus for injecting blood into the recipient. Note the direction of arrows and pump and compare with Figure 11. This arrangement produces positive pressure within the flask. Keeping the manometer between 70 and 100 mm. gives the most satisfactory flow.

fully polished with "Bon Ami" or a similar preparation preceding sterilization, as the authors have found that the blood flows much more freely when the needles are so cleaned. The authors are using a blood-pressure apparatus as a tourniquet on the donor's arm, which is an excellent method for regulating the pressure so as

to get the maximum flow of blood. They have found that a pressure slightly lower than the donor's diastolic pressure usually gives this result.

The needle connected with tube A is introduced into the vein of the donor, and at the same time a small amount of suction is applied. As the blood flows, the flask is gently agitated. When the desired amount is obtained, the needle is withdrawn and is immediately placed into a small amount of sodium citrate solution which is drawn up through the tube, thereby cleansing this part of the system. The needle is now removed and the spring manometer is attached in its place. The pump is now disconnected and reversed (Fig. 12); the direction is indicated by arrows in the illustrations. Air is pumped into the flask, forcing the blood through the tube B going to the recipient, filling this part of the system. When the air has all been expelled from the tube B, it is clamped; and the needle is inserted into the patient's vein. The clamp is removed and the blood is injected by producing positive pressure in the flask.

The blood should be injected at the rate of 100 c.c. every six minutes; *i. e.*, 500 c.c. in a half hour. The pressure that is necessary to do this depends on the size of the needle used and the pressure within the vein. By the use of the manometer, this can be readily determined and subsequently kept at the optimum point. It is usually in the neighborhood of from 70 to 100 mm. of mercury.

Except in cases of great depletion by hemorrhage, the authors believe that small amounts of blood frequently given are preferable to larger amounts given at longer intervals, from 300 to 500 c.c. being the amount usually used.

Simple Blood Transfusion Apparatus. Barnett Greenhouse⁹ suggests the use of a three-way stopcock and syringe as shown in Figure 13.

"The apparatus as sketched is ready to receive the donor's blood, since Bore A is in direct communication with the donor's needle and the syringe, while Bore B is closed. After the syringe is filled by drawing out the piston the stopcock is turned halfway around. This

(9) Jour. Amer. Med. Ass'n., Sept. 25, 1920.

at once shuts off Bore A and places Bore B in direct communication with the syringe and the recipient's needle. The blood is then forced into the recipient's vein by pushing in the piston. The process is repeated until sufficient blood is transfused."

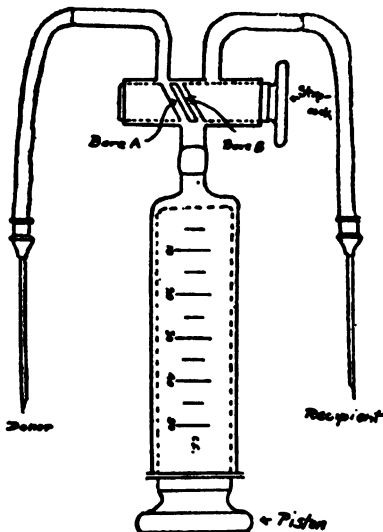


Fig. 13. Direct blood transfusion apparatus, with three-stopcock.

CARBON DIOXIDE

Carbon Dioxide Inhalation in Acapnia. Y. Henderson, H. W. Haggard, and R. C. Coburn¹ believe that CO₂ inhalation is of great value in acapnia, a diminution of the store of carbon dioxide in the blood and tissues which induces profound functional disturbances. To employ it successfully, however, we must distinguish between the two forms of low blood alkali. A low bicarbonate content may be due to either the acidotic process or the acapnial process. In the former, the alkali is first neutralized by acids entering the blood, and the carbon dioxide falls secondarily. In the latter, the

(1) Jour. Amer. Med. Ass'n., Aug. 6, 1921.

respiration is primarily excited; carbon dioxide is blown off, and it is now the alkali which falls secondarily as a compensation. Both result in a low blood alkali, but in all fundamental aspects they are antithetical. If over-breathing is prolonged, alkali soon begins to leave the blood. This apparently is Nature's method of preventing the alkalosis from becoming extreme. If urine is being secreted, it becomes alkaline and thus carries away a part. Apparently, however, most of the alkali passes into the tissues to be there stored, in some way as yet not fully understood, until recalled to the blood. Thus, the condition of acapnia and tissue alkalosis induces a low blood alkali. Unlike the acidotic state, however, the alkali has not been neutralized, but has been forced out of the blood in the effort of the organism to combat an otherwise too acute alkalosis. The normal man who voluntarily over-breathes for a moment or two, thus inducing a slight acapnia, has in consequence a period of apnea. Similarly, but in greater degree, the patient, who by unskillful etherization is kept in respiratory excitement for ten or fifteen minutes or more, would inevitably exhibit subsequently an alarming or even fatal respiratory failure, if it were not for the compensatory passage of alkali out of his blood. However, if the blood alkali has been greatly reduced, a condition of profound depression may continue for hours, before the organism succeeds in re-accumulating the needed carbon dioxide and recalling alkali to the blood. In this depression, the blood stagnates—probably in the abdominal vessels and viscera. The skin vessels are constricted. The superficial veins become scarcely visible, or disappear. The venous return to the right heart is deficient; the cardiac action lacks adequate volume, and arterial pressure is low. Respiration is so much depressed that the oxygen intake is impeded and cyanosis is evident. The reason is merely that, as carbon dioxide is the normal stimulus for breathing, and as the store of this substance within the body has been greatly reduced, normal breathing can not return until a sufficient amount of carbon dioxide has re-accumulated in the blood and tissues. The vital depression probably decreases also the production of carbon dioxide. Mean-

while, anesthesia continues to a greater or less extent, for the elimination of ether is through the lungs, and the rate of elimination depends, therefore, on the volume of the pulmonary ventilation. Full breathing is as essential to rapid termination of anesthesia as it is to rapid induction.

Obviously the natural method of treatment to assist Nature to recover the normal equilibrium, is by restoring the carbon dioxide. Thereby we reverse the acapnial process. All this is accomplished effectively by an inhalation device, by means of which any desired amount of carbon dioxide may be administered to the patient mixed with the inspired air, but with no appreciable degree of rebreathing, as rebreathing would impede the elimination of ether. When a patient is so treated, the first response is an augmentation in the volume of breathing. Until this is obtained, the amount of carbon dioxide administered must be adjusted with caution. With a little experience one learns how to push the dosage from this point on; and at this stage, it should be pushed. In a few minutes arterial pressure begins to improve. The skin loses its leaden hue and becomes pink as the small vessels relax and fill; and the veins of the arms and neck begin to show again. From this point on, the administration of the gas is reduced, so as not to push the circulation too hard. By care in watching the distension of the superficial veins and adjusting the inhalation accordingly, we avoid an over-supply of blood to the right heart by the augmented venous return. Meanwhile the active pulmonary ventilation has rapidly aerated the greater part of the anesthetic out of the blood. In some cases after only fifteen or twenty minutes the patient is conscious, and after a few minutes more the administration of carbon dioxide may be stopped. On the other hand, in animals in which the alkali reserve has been diminished by intravenous injection of acid, the administration of carbon dioxide does not recall a normal amount of alkali to the blood. It cannot, for the alkali no longer exists in the body. Indeed, such an animal when treated with carbon dioxide is overwhelmed by the acidosis, and usually dies.

Carbon Dioxide and Oxygen Inhalation in Poisoning with Carbon Monoxide. What might be a most important contribution to the treatment of illuminating gas poisoning is the advocacy by Y. Henderson and H. W. Haggard² of the addition of CO_2 to the oxygen inhalation in illuminating gas poisoning. The authors believe that during carbon monoxide poisoning a great deficiency of CO_2 occurs in the blood owing in the first place to a vigorous hyperpnea, and secondly to diminished production of CO_2 by reason of deficient oxygenation and

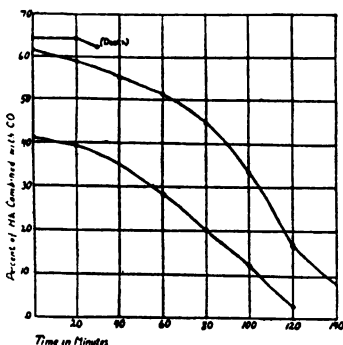


Fig. 14. Plotted from data of experiments 1, 2, 3. Showing the rate of elimination of carbon monoxide from the blood of profoundly asphyxiated but thereafter untreated animals.

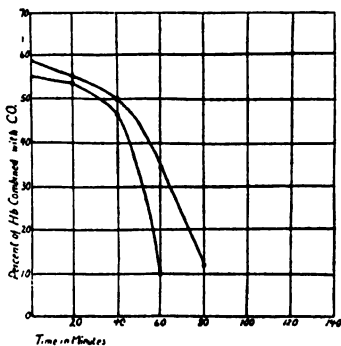


Fig. 15. Plotted from the data of experiments 4 and 5. Showing the rate of elimination of carbon monoxide from the blood of animals under inhalation of oxygen.

muscular depression. As the result of this deficiency of CO_2 in the blood, asphyxiated animals, when restored to pure air, exhibit for half an hour or more very poor respiration and it is found that the rate of elimination of carbon monoxide is correspondingly slow (Fig. 14), the condition of tissue asphyxiation is thus continued, although the body is surrounded by fresh air. The authors believe that this post-gassing period of continued asphyxia may be of critical importance in inducing subsequent structural degenerations and functional impairments. Its abbreviation is therefore an important

object both for therapy and prophylaxis. Oxygen inhalation during this period has only a slight effect (Fig. 15); it is not adequately inspired. Inhalation of CO₂ diluted with air has an immediate effect in augmenting breathing and hastening the elimination of carbon dioxide (Fig. 16). The best effects are obtained when oxygen is inhaled to which 10 per cent. of CO₂ has been added (Fig. 17). The augmented breathing allows the oxygen to effect a rapid displacement of carbon monoxide from the blood. Within five minutes the animals were

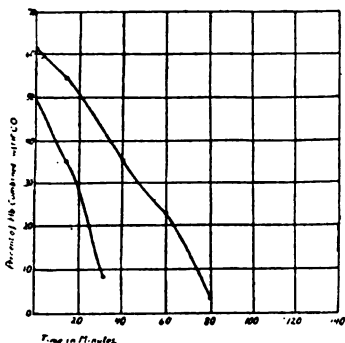


Fig. 16. Plotted from the data of experiments 6 and 7. Showing the rate of elimination of carbon monoxide from the blood of animals while breathing air plus CO₂.

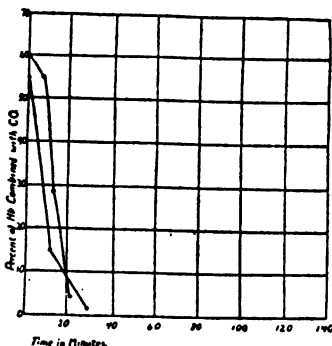


Fig. 17. Plotted from the data of experiments 8 and 9. Showing the rate of elimination of carbon monoxide from the blood of animals under inhalation of oxygen plus CO₂.

conscious and struggling and almost normal within thirty minutes; while animals without treatment were unconscious for almost an hour and still unsteady for several hours.

[Henderson and his associates have published the description of an apparatus for CO₂ inhalation, which was abstracted in Practical Medicine Series, 1920, Vol. VI, p. 99.—Ed.]

DIET

The Principle Underlying Adjustment of Diet in Diabetes. R. T. Woodyatt³ has contributed a most

(3) Archiv. Int. Med., August, 1921.

illuminating article on this subject. By descending to the fundamentals, he has succeeded in clarifying what may seem to many a mystery: the success of such treatments as Donkin's "milk cure," von Duering's "rice-butter" cure, Moss's "potatoe" cure, von Noorden's "oatmeal" cure, or Falta's "cereal" cure. He also shows the undesirability of prolonged starvation as a method of treatment of diabetes.

Fasting in cases of a sufficiently emaciated patient is equivalent to a pure protein ration. Inasmuch as 100 gm. of protein yields in the body 58 gm. of glucose, and perhaps 48 gm. of fatty acid, a starving diabetic with low sugar tolerance may continue to excrete sugar and be in a state of acidosis on starvation treatment. If such a patient be given enough fat to reduce the protein catabolism, this will reduce the quantity of glucose thrown into the circulation. An opportunity is thus given to introduce more carbohydrate in the diet, which still further lowers the protein breakdown. The author cites an illustrative case in which this actually happened: a patient in whom the "rice-butter" diet (containing 24 gm. carbohydrate, 2.5 gm. protein, 102 gm. fat, and 1,024 calories) afforded the patient all he could eat, relieved the acidosis and made the urine almost sugar-free, after a nine weeks' trial of the ordinary practice of under-nutrition had failed to establish a non-diabetic state. A further adjustment of the diet, by adding eggs and other protein so as to put the patient into nitrogen equilibrium and slightly increasing the amount of carbohydrate and giving a still more liberal allowance of fat, rendered the patient's urine free of sugar and of acetone.

If a patient has plenty of fat in his body, he will burn much tissue fat and much less protein. In such a patient the ingestion of the right quantity of fat will save the necessity of drawing on his own tissue fat. Why, asks Woodyatt, should we compel a patient to consume his own fat for the purpose of desugarization, when we might supply the fat in the diet, especially as, in drawing from his tissues, he lowers his fat reserves and to that extent increases his protein losses. Of course, if too much fat is ingested this would aggravate acidosis and

increase the protein loss; but in the right quantities it simply replaces tissue fat.

To determine the quantity of fat that might be introduced without danger of acidosis, it is necessary for us to remember that this condition appears as the result of oxidation of fatty acid in the absence of a sufficient proportion of "oxidizing" glucose. The ratio required appears to be that F A : G shall not exceed 1.5. When we know the quantity of glucose that the patient can utilize, we must, in order to secure for him the maximal number of calories, give every possible gram of fat that he can use in accordance with the ratio given, while the protein must be kept as low as possible and the carbohydrate as high as possible; this because each gram of glucose not only provides 4 calories, but also makes possible a normal oxidation of 1.5 gm. of higher fatty acid. On the other hand, 1 gm. of protein, having the same caloric value as the carbohydrate, yields less glucose to support fat combustion and besides this liberates fatty acid.

For mental calculation, Woodyatt proposes the following rule: If one knows that a patient can actually utilize a certain number of grams of glucose, take this number times 17 as the approximate number of calories that he will be capable of using at best, without glycosuria or acetonuria, if the diet is most favorably balanced. Then, knowing the patient's weight, the severity or mildness of the situation becomes apparent.

Diabetic Diet Table for Patient's Use. Ephraim M. Ewing⁴ has devised a table to make it easy for the diabetic layman to calculate the amount of food suited to him. We now know that we must reckon the daily quota of protein and fat, as well as of carbohydrate. In this diet list each portion in the protein table contains approximately 6 gm. of protein, this quantity being chosen because it is the protein content of eggs, certain diabetic muffins, rolls, etc. Each of the carbohydrate portions contains approximately 5 gm.

[Approximately the amount contained in one Uneeda cracker.—ED.]

(4) Jour. Amer. Med. Ass'n., Jan. 29, 1921.

DIABETIC DIETARY

| A. Protein equivalents (6 gm. each): | Weight of | Protein | Fat | Carbo- hydrate |
|---|-----------------|---------|-----|-------------------|
| | Portion, Gm. | | | |
| Lean meat, poultry, cooked..... | 22 | 6 | 3 | 0 |
| Roast, medium fat..... | 22 | 6 | 6 | 0 |
| Fish, lean (cod, haddock, etc.)..... | 30 | 6 | 0 | 0 |
| Fish, fat (salmon, shad, etc.)..... | 30 | 6 | 3 | 0 |
| Oysters, six average..... | .. | 6 | 1 | 3 |
| Ham, boiled, sliced..... | 30 | 6 | 7 | 0 |
| Bacon..... | 36 | 6 | 18 | 0 |
| Pork sausage..... | 30 | 6 | 10 | 0 |
| Beef soup (not greasy)..... | 150 | 6 | 1 | 1.5 |
| Egg, one..... | 60 | 6 | 6 | 0 |
| Egg white, two..... | .. | 6 | 0 | 0 |
| Egg yolk, two..... | .. | 6 | 12 | 0 |
| Cheese, American..... | 20 | 6 | 7 | 0 |
| Cheese, cottage..... | 30 | 6 | 0 | 1 |
| Casein flour muffin (Joelin), one..... | .. | 6 | 6 | 0 |
| Calf's foot jelly (with saccharin)..... | 45 | 6 | 0 | 0 |
| Milk, three-fifths glass..... | 150 | 6 | 6 | 7 |
| Almonds, walnuts..... | 30 | 6 | 18 | 5 |
| Brasil nuts..... | 35 | 6 | 24 | 2 |
| Peanuts..... | 25 | 6 | 9 | 5 |
| Pecans..... | 45 | 6 | 31 | 6 |
| B. Carbohydrate equivalents (5 gm. each): | | | | |
| Asparagus, cabbage, celery, chard, cauliflow- er, cucumber, eggplant, grape- fruit, greens, leeks, lettuce, okra, radishes, rhubarb, stringbeans, spin- ach, sprouts, tomato..... | 150 | 2 | 0 | 5 |
| Beets, carrots, mushrooms, onions, squash, turnips..... | 75 | 1 | 0 | 5 |
| Canned lima beans, green peas, parsnips | 35 | 1 | 0 | 5 |
| Green lima beans, green corn..... | 25 | 1 | 0 | 5 |
| Orange, one half small..... | 75 | 0 | 0 | 5 |
| Lemon juice..... | 50 | 0 | 0 | 5 |
| Blackberries, cranberries, muskmelon, peach, pineapple, strawberries..... | 75 | 0 | 0 | 5 |
| Alligator pear..... | 75 | 1 | 15 | 5 |
| Apricots, cherries, huckleberries, pear, raspberries..... | 30 | 0 | 0 | 5 |
| Apple, banana, grapes, plums, prunes... | 25 | 0 | 0 | 5 |
| Oatmeal, boiled..... | 45 | 1 | 0 | 5 |
| Oatmeal, dry..... | 8 | 1 | 0 | 5 |
| Wheat cereal porridge..... | 30 | 1 | 0 | 5 |
| Macaroni, hominy, boiled; potato, baked, boiled; rice, boiled..... | 25 | 0.5 | 0 | 5 |
| Baked beans, canned..... | 25 | 2 | 0.5 | |
| Bread..... | 9 | 1 | 0 | |
| Cracker..... | 7 | 0.5 | 0 | 5 |
| Olives, green..... | 60 | 0.5 | 10 | 5 |
| Cream, 20 per cent..... | 150 | 5 | 30 | 5 |
| Cream, 40 per cent..... | 150 | 5 | 60 | 5 |
| Milk, one half glass..... | 120 | 4 | 5 | 5 |
| Wheat flour, 75 per cent. carbohydrate | | | | |
| Molasses, 70 per cent carbohydrate | | | | |
| Sugar, 100 per cent. carbohydrate | | | | |
| C. Portions by which fat may easily be added: | | | | |
| Butter, 85 per cent. fat (3 parts)..... | 30 | 0 | 25 | 0 |
| Olive oil, lard, etc., 95 to 100 per cent. fat (1 level tablespoonful)..... | 15 | 0 | 15 | 0 |
| Mayonnaise, home-made (1 level table- spoonful)..... | 15 | 0 | 15 | 0 |
| Bacon, cooked..... | 36 | 6 | 18 | 0 |
| Cream, 20 per cent. (1 level table- spoonful)..... | 15 | 0.5 | 6 | 0.5 |

| | Weight of Portion, Gm. | Protein | Fat | Carbo- (hydrate) |
|---|------------------------------|---------|-----|---------------------|
| Cream, 40 per cent. (1 level tablespoon- ful)..... | 15 | 0.5 | 12 | 0.5 |
| Alligator pear..... | 100 | 2 | 30 | 7 |
| Nuts, olives, etc. (see above) | | | | |

D. Miscellaneous (to be added at the physician's discretion):

These articles may be added to the dietary without allowing for their food value: coffee, tea, washed bran, agar agar, cellulose flour, saccharin, liquid petrolatum (instead of lard), etc. To obtain the total number of calories multiply the total grams of protein by 4, of fat by 9, and of carbohydrate by 4, and add the results. The average daily requirement is 10 to 15 calories per pound (25 to 35 per kilogram).

It is believed that the following advantages are offered by the present arrangement:

1. Substitution of one food for another requires no arithmetic. So variety, one of the diabetic's chief desires, is made as easily attainable as possible.

2. With such a dietary, metric scales and knowledge of simple addition, it is easy for even the uneducated person to limit himself to the prescribed number of grams of protein, fat and carbohydrate. For instance, if a patient's prescription reads: protein 65 gm. carbohydrate, 35 gm., and fat, 150 gm., he may be told to weigh on his scales nine or ten protein portions, and seven carbohydrate portions (which also contain some protein), marking down the protein, fat and carbohydrate content in each case. After these figures have been added, the required amount of fat is weighed or measured.

Sugar-Free Cream for Diabetic Patients. Florence H. Smith and W. D. Sansum⁴ have modified the method described by Williamson, which consists in adding to a pint of water 3 or 4 tablespoons of fresh cream and skimming off the fatty water after from twelve to twenty-four hours, by using a dairy cream separator for the immediate skimming of cream from similar but larger mixtures of cream and water. The loss of sugar and salts alters the flavor of the cream. This may be practically restored by the addition of the proper amount of common salt, from 0.5 to 0.7 per cent. and a small amount of saccharin. The saccharin should be added just before serving, since it becomes bitter if in solution for a long time. Any dairy can prepare such

(4) Jour. Amer. Med. Ass'n., March 19, 1921.

cream. The product is an economical one. Its keeping qualities are excellent. Samples have been kept in the icebox for weeks with no apparent change in flavor.

Diet and Other Measures in Simple Anemia. H. G. Whipple, F. S. Robscheit, and C. W. Hooper⁵ report the result of extensive feeding experiments in dogs rendered anemic by bleeding them one-fourth of the determined blood volume on each of two successive days. Under these conditions a diet of mixed table scraps will effect complete blood regeneration in a period of from four to seven weeks. During sugar diet periods the regeneration of hemoglobin and red blood cells is distinctly less than during fasting. This the authors believe may be due to the carbohydrate protection of body protein during katabolism, which shows that certain protein fractions that may be recast into hemoglobin are lacking. Histidine given with sugar appears to cause the production of hemoglobin over the control level. This amino acid may be one of the important elements in the hemoglobin regeneration complex. A restricted diet of bread and milk barely sufficient for body maintenance will rarely permit of complete blood regeneration following simple anemia. A liberal diet of this type will often suffice for complete blood regeneration. Crackermeal, rice, or potatoes and milk make up a diet which may be classed with bread and milk as regards its influence upon blood regeneration.

Cooked lean beef and beef heart alone or in combination with other foods give a rapid blood regeneration after anemia. Three or four weeks of such diet will completely repair an anemia of standard degree. Cooked liver has been found even more effective; blood regeneration may be completed in from two to four weeks. Commercial meat extract is inert, and watery liver extract has but little influence upon blood regeneration. Blaud's pills are inert when added to various diets which do or do not favor rapid blood regeneration. Hemoglobin (by mouth, intravenously or intraperitoneally) exerts a distinctly favorable influence upon subsequent blood regeneration.

(5) Amer. Jour. Physiol., September, 1920.

Principles of Diet in Tuberculosis. W. S. McCann, and D. P. Barr⁶ consider forced feeding unnecessary and probably harmful in the active stages of pulmonary disease. Since protein increases the respiratory exchange, in the tuberculous as well as in the normal individual, it may be well to limit the protein intake during the period of activity of tuberculosis in order to put the lungs at rest. The authors found that the basal metabolism of tuberculous patients may be normal or very slightly above that of normal men of the same size. Fever increases the metabolism, but this increase is not great.

VITAMINES

The Influence of Heat and Oxidation upon Vitamines. Having observed that boiled milk was practically equal in nutritive properties to the unheated raw milk, while pasteurized milk, heated at 145° F. for thirty minutes, produced scurvy very quickly, E. V. Anderson, R. Dutcher, C. H. Eckles, and J. W. Wilbur⁷ discovered that the pasteurized milk had been stirred rather violently with motor-driven propellers, while the boiled milk had not been stirred mechanically. This led these investigators to believe that oxidation had occurred in the pasteurized milk due to the intimate contact of air with the milk particles. Consequently, as a result of work on many guinea-pigs, they were able to show that the nutritive and antiscorbutic properties of cow's milk are destroyed by oxidation. Some destruction occurs when air is bubbled through milk at 145° F. for thirty minutes, but the destruction is much more marked when oxygen or hydrogen peroxide is used. Oxygen and hydrogen peroxide will destroy the antiscorbutic accessory at room temperature although the destructive action is hastened as the temperature increases. Milk may be pasteurized in closed vessels or boiled in the open air without appearing to lose its nutritive and antiscorbutic properties when fed to guinea-pigs. When carbon diox-

(6) *Archiv. Int. Med.*, December, 1920.

(7) *Science*, May 6, 1921.

ide is bubbled through the milk, it compares very favorably in nutritive properties with the raw milk.

Work now in progress, on orange juice shows that the antiscorbutic properties are not destroyed by boiling for thirty minutes. At least, if destruction occurs, it is not discernible with the methods employed. Hydrogen peroxide destroys the antiscorbutic factor in orange juice at room temperature, and the speed of the oxidation is hastened as the temperature increases. Oxidation would appear to be a more important factor than heating so far as the nutritive and antiscorbutic properties of milk are concerned.

Yeast Useless in Infant Feeding. Maynard Ladd⁸ cautions us not to apply the conclusion reached as a result of feeding laboratory animals too directly to infants. Milk is not a natural food for these experimental animals, except for very limited periods, if at all. In view of the advertisements in some medical journals and the fact that certain commercial firms are taking advantage of the present interest in vitamins to put into the hands of the physicians and of the public generally products which, on the basis of animal experiments, were recommended as valuable growth promoters for the human infant, there is danger that the general practitioner will be directed away from the principles of sound and scientific feeding. Ten babies, all difficult feeders, were carefully observed for different periods. The weight charts give evidence of satisfactory development but careful analysis of the rate of weight development during the periods with yeast and without yeast do not show any benefit that can be attributed to the yeast itself. One child developed furunculosis while taking the yeast, obviously from contact with a baby similarly affected, and in that case it had no prophylactic value. Ill effects were observed in one baby who developed severe fermentative diarrhea soon after the yeast was begun; later, when this was corrected, it took another dose with no bad effects, but still without benefit to its nutrition.

The Value of Cod-Liver Oil. While clinical observers have always been positive of the therapeutic

value of cod-liver oil, they have been unable to give any explanation for its superiority to other oils. Recent research upon vitamins has thrown an entirely new light upon the action of cod-liver oil, for it has shown that crude cod-liver oil is peculiar in containing a far larger amount of the fat-soluble vitamin A than any other foodstuff. An editorial in the *British Medical Journal*, Aug. 13, 1921, summarizes what is known about cod-liver oil as a source of vitamin A.

Animals are unable to synthesize the vitamin A contained in their fats; they obtain supplies from vegetable foods and store the vitamin in their fat. Adult animals contain a large reserve of the vitamin, in their fat, and can live on these supplies for prolonged periods. Therefore, it is not easy to produce any very obvious effects upon adult animals by deprivation of vitamin A. Young growing animals require much larger amounts of this vitamin and have smaller reserves, and in these deficiency of vitamin A produces effects in a few weeks or months.

Vitamin A is contained in the green leaves and the growing parts of plants, and it is from these that the animal world ultimately obtains its supply of vitamins. Vitamin A is stored by animals in their fats, and occurs in large quantities in milk fat and in egg yolk. The fats and oils of fishes and of whales also contain an exceptionally large amount of this vitamin. All the vitamin A present in milk is contained in the milk fat; there is, therefore, very little in skimmed milk. The vitamin A content of milk depends entirely upon the diet of the animal, and vitamin A may be almost completely absent from the milk of stall-fed cows. Similarly, it may be absent from the milk of women fed on a diet free from vitamins. The vitamin content of milk is reduced by pasteurization or by boiling; and both condensed and dried milk contain smaller amounts of the vitamin than does fresh milk. Lard as ordinarily manufactured contains no vitamin. Vegetable oils and fats contain little or none of the vitamin. The absence of vitamin A from the diet can be shown to produce in animals the following effects:

1. Lack of growth in young rats (Hopkins, Drummond, and others).
2. Rickets in puppies (Mellanby).
3. Disorders of dentition in puppies (Mellanby).
4. Diminished resistance to infections.
5. Failure of the nutrition of the cornea resulting in xerophthalmia.
6. Tendency to edema.

The following diseases are all believed to be related to lack of vitamine A in man: rickets, osteomalacia, keratomalacia, and war edema. Deficiency of vitamine A is very possibly also an important cause of dental caries and impaired growth. The etiology of rickets is a question of enormous sociologic importance, and controversy has arisen concerning Mellanby's conclusion that rickets is a deficiency disease caused by deficiency in a factor which has the same distribution as vitamine A. However, the tragic experience of Central Europe furnishes a striking proof that rickets is a deficiency disease, for Dalyell states that 100 per cent. of infants of nine months in Vienna have rickets, and since the climate and housing conditions of Vienna are the same as in 1914, this result must be due to malnutrition; moreover, since a large proportion of the Viennese children are breast-fed, the rickets must be due to maternal malnutrition. Strikingly beneficial results have been obtained from the administration of cod-liver oil in all of the diseases attributed to lack of vitamine A. The addition of cod-liver oil to the diet of the mother in breast-fed infants in Vienna produced a most striking beneficial effect upon the rate of growth. Hess believes that cod-liver oil given in full doses, and not rendered impotent by excessive refining, is almost a specific in the treatment of rickets. There is also strong evidence that keratomalacia and hunger edema are cured by cod-liver oil. In none of these is a similar effect produced by vegetable fats. Hence, the only probable explanation is that the specific action of cod-liver oil is due to its high content of vitamine A. The most striking results with cod-liver oil have been obtained in the starving populations of Central Europe, but there is strong evidence that lack of

vitamine A is an important factor in producing disease in urban populations under normal conditions. While this vitamine is contained in whole-meal bread and in butter, it is absent from white bread and margarine. It occurs in fresh meat, but tinned meat contains little or none. Thus a diet of white bread, margarine, jam, and salt fish or tinned meat is therefore almost free from vitamine.

Zilwa and Miura found that crude cod-liver oil contained no less than 250 times as much vitamine A as butter, but that the refined oil contained much less vitamine, although its activity was superior to that of butter. However, cod-liver oil may be crude and unpalatable owing to one of two causes; the oil may have undergone no refining process, and therefore, contain the full vitamine content; on the other hand, it may be unpalatable because excessive putrefaction of the livers has been allowed to occur before extraction, so that the resulting oil is so impure that it can not be fully purified; such an oil will probably contain no vitamine at all.

Vitamine Food Tablets. J. F. McClendon⁸ recommends for persons who do not, under the present system, receive sufficient vitamins in their food, or whose dietary habits form an obstacle to the consumption of sufficient vitamins, the peel of citrus fruits as it is very rich in vitamins. The use of such peel in tablets [or capsules—Ed.] that may be swallowed whole, seems desirable in order to avoid the censorship of the palate. Orange peelings ground in a meat chopper, dried, and then ground in a coffee mill may be made into tablets by the addition of dehydrated orange juice acting as a binder. Such tablets contain vitamins A, B and C. Ground spinach may be similarly made into tablets with orange juice.

BACTERIOTHERAPY

Feeding of Bacteria Produces Only Temporary Change in Intestinal Flora. W. Klein⁹ fed white mice and guinea-pigs with a strain of *Bacillus coli* that was

(8) Science, Oct. 28, 1921.

(9) Therap. Halbmonatsh., Dec. 15, 1920.

capable of growing luxuriously in 1:1000 malachite green. Ordinary strains of *B. coli* can not grow or grow but sparingly in a dilution of 1:4000 of the dye. Inasmuch as malachite-green-fast *B. coli* are occasionally found in the alimentary tract of mice and guinea-pigs, such organisms must be considered potentially natural to these animals. Indeed, a number of animals had to be eliminated from the experiment because preliminary tests of the feces showed relatively malachite-green-fast colon bacilli.

Employing the maximum tolerated dose of these organisms, the author found it impossible to recover the introduced germs for more than eight or nine days after the feeding. When the bowel was injured by powdered glass, croton oil, or tincture of opium, alongside of the bacterial feeding, the length of elimination was increased to between thirteen and seventeen days. Change of diet by feeding meat or placenta increased elimination to thirty-four days. On the other hand, feeding the animal's stool after bacterial administration did not increase the elimination period to any marked extent. Attempts to combine bacterial feeding and immunization did not give uniform results. But in one case the germs introduced were found after 165 days.

The author arrives at the conclusion that permanent implantation of organisms can not be produced under the various conditions established in his experiments. In this his work is in agreement with that of numerous other observers. It is all the more remarkable that, with the constancy of the normal bacterial flora of the feces, a sudden change should take place in it as is known to occur in certain infectious diseases such as typhoid fever, dysentery, and cholera, also that such abnormal organisms remain in the stool in certain cases for an indefinite length of time after recovery from the disease producing the "carrier state." We are evidently not yet familiar with an important link in the chain of events resulting in bacterial implantation in the intestine. There is little doubt that it is to be looked for in the domain of immunology.

[These experiments do not lend encouragement to the attempt to cure the carrier state by the ingestion of the

bacteria or to the hope of permanently curing patients suffering from other forms of abnormal flora by this kind of bacterial therapy. They do not, on the other hand, preclude the possibility that massive feeding of such organisms as the lactic-acid bacillus, together with radical change in diet may not at least temporarily produce an improvement in the intestinal conditions and amelioration of symptoms in certain cases of bacterial enteric disturbance.—Ed.]

ANTIGEN THERAPY

(A) SPECIFIC ANTIGEN THERAPY

Antigen Therapy. H. L. Lyon-Smith¹ urges the use of the word "antigen," coined to indicate "any substance which gives rise to an antibody" as a more expressive word than "vaccine."² He points out the interesting fact that one may give, in most cases, large doses of the wrong vaccine with very little harm; but, when a correct diagnosis of the infecting organisms has been made, then an overdose of the right vaccine will produce injurious hypersensitiveness and may make the patient worse for a few weeks.

Archibald McKendrick³ argues against a preconceived, rule-of-thumb, "course" of vaccines as unscientific, and liable to lead to disappointment. The dosage of any vaccine must be regulated by the reaction of the patient, and by this alone. A decided reaction should be an indication for diminution in, or even deferring, the following dose.

C. E. Jenkins⁴ advises against the use of autogenous vaccines for prophylactic purposes. That an autogenous vaccine is superior to a stock vaccine as a curative agent is well known. Stock vaccine, on the other hand, is recognized as the proper type to use for prophylaxis. For example, the sufferers from recurrent acute catarrh of the

(1) Practitioner, August, 1921.

(2) The word "Vaccine," being derived from Latin *vacca*, a cow, applies properly only to cowpox virus. To speak of an "autogenous vaccine" when the material is derived from a human being and not a cow is, to say the least, paradoxical.—Ed.

(3) Practitioner, August, 1921.

(4) *Ibid.*

upper respiratory passages can be divided into two main groups. In the first group, probably the smaller, the patients have a permanent chronic catarrh of varying intensity, and are subject to periodical acute exacerbations, usually brought on by climatic change or exposure. An autogenous vaccine is the correct type to use for these cases, because the condition is always present and the vaccine is required for *curative* purposes. The second and larger group comprises those persons who are usually free from any sign of catarrh, but who invariably "catch cold" if brought into contact with anyone suffering from an acute catarrh. An autogenous vaccine would only protect the patient against future attacks caused by the same organism. But the autogenous vaccine under consideration would have no power to protect against any of the other organisms. A mixed stock vaccine is free from this objection. It is designed to protect against all the common catarrhal organisms, and is based upon the reasonable assumption that the causal organism of the patient's next attack will fall within its area of protection.

Antigen Therapy in General Practice. Alexander Fleming⁵ who has been practicing vaccine therapy since it was in its infancy, finds himself as time goes on more and more convinced of its efficacy, not only for the more severe cases which are to be seen at a hospital, but also and more especially for the lesser ailments which seldom appear in hospitals, but with which the practitioner has much to do.

Fleming gives the following rules on the use of stock vaccine versus autogenous vaccine:

In many cases in which the infecting organism is easy to cultivate and the vaccine is easy to prepare, it is less trouble to make an autogenous vaccine than it is to identify the organism exactly. On the other hand, the isolation of the microbe and the preparation of the vaccine is frequently a very tedious and laborious proceeding; and in such cases, if the nature of the infecting agent is obvious, a stock vaccine is often employed and an autogenous vaccine made only if the stock vaccine fails. Of course, stock vaccine is employed where

(5) Brit. Med. Jour., Feb. 19, 1921.

the vaccine is to be used for prophylaxis. The fact that stock vaccines have been used with such signal success in the prophylaxis of typhoid, paratyphoid, cholera, plague, and the catarrhal infections of the respiratory tract, is of the utmost importance in that it shows that it is not necessary to insist on a vaccine being made of a microbe of exactly the same parentage as the infecting microbe so long as it belongs to the same species. Where the nature of the bacterial infection is known but a culture of the microbe can not readily be obtained from the patient, as in tuberculous infections or where the infection is deep-seated—for instance, in the joints or glands—there is almost no choice; and we have to use stock vaccines. The results obtained with these in such cases also show that good immunizing responses can be induced. Where, owing to the profusion of contaminating microbes, it is difficult to identify and differentiate with sufficient sharpness one microbe from another of the same morphologic species, as in chronic catarrhal conditions of the respiratory and alimentary tracts, in putrid infections of wounds, and in the erosions often associated with malignant tumors, it is advisable to employ the polyvalent stock vaccines made from a large number of strains of the microbes in question, especially as the stock vaccine can be prepared from cases in which there is no doubt as to the nature of the infection.

Where the infecting microbe can easily be obtained from the patient in pure culture we have to balance the possible advantage of an autogenous vaccine against the labor and expense involved in procuring it. In staphylococcus infections, a stock vaccine will in almost all cases give as good results and sometimes prove the more beneficial. Likewise, *Streptococcus pyogenes* vaccine is one of the most effective of the stock vaccines. Pneumococci have recently been split up by immunologic methods into three or four subgroups, and it is essential that a stock vaccine of these organisms should contain representatives of all the groups. When this is done stock vaccines of these organisms are very effective. On the other hand, with *B. proteus* and Pfeiffer's bacillus, an autogenous vaccine should be preferable. It is desirable to use an autogenous vaccine when (a) the infecting

agent belongs to an ill-defined group of microbes as in the so-called, "*B. coli* infections." (b) When the infection is severe and it is felt to be too great a risk to wait to see whether the stock vaccine is effective. It is wise in such cases to give a small dose of the stock vaccine while the autogenous one is being prepared. (c) When treatment with a stock vaccine has failed.

Clinical effects of a bacterial vaccine may be divided into two classes: (a) toxic and (b) immunizatory. Toxic effects follow soon after the injection and the term "reaction" is applied to them. They fall under three headings:

1. Local Reaction.—This is always more severe when the injection is made in a region which is subject to pressure of the clothing, or which does not contain much subcutaneous fat, and is situated over muscles which are constantly in use (for example, the forearm). The best sites for inoculation seem to be in women about two inches below the center of the clavicle or behind the shoulder; and in men the flank also is very suitable.

2. Focal Reaction.—With a small dose there is no apparent focal reaction. With a larger dose there is some increase of the inflammatory signs in the infected focus. With a very large dose there may be a very great exacerbation of the symptoms which may result in the necrosis of the infected tissues.

3. General Reaction.—Small doses of vaccine are not followed by general toxic manifestations, but very large doses are very apt to be followed after a few hours by signs of a general intoxication. A mild general reaction consists merely of a little malaise, but if the reaction is severe then there may be rigors, sweating, high fever, and even diarrhea, sickness or collapse. Doses of vaccine causing severe reactions should never be used. This general reaction is caused in part by the toxic substances which are introduced in the vaccine, but it is also probably caused largely by the absorption of toxic material from the infected focus, which has at the same time been much disturbed by the focal reaction.

Immunizatory Phenomena: 1. Focal changes vary so much in their character that it is not possible to generalize further than to say that after twelve hours or

longer there is a diminution in the inflammatory symptoms.

2. General: Usually the first beneficial effect following the administration of a vaccine is a feeling of well-being in the patient. When small doses are used this may follow within an hour or two, and it is frequently very striking. When the patient is running a slight temperature a small dose of vaccine administered in the morning will bring the temperature down the same evening. This fall in the temperature coincides with a rise in the antibacterial content of the blood (Fig. 18).

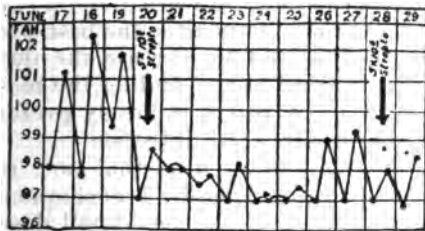


Fig. 18. The patient to whom this chart refers was suffering from a septic compound fracture of the femur, and for about three weeks had had a septic type of temperature similar to that for the three days indicated in the chart previous to the inoculation.

The dosage of vaccines is, in general, the maximum dose which will not give rise to a general reaction in the patient. The more severe the infection the smaller should be the dose of vaccine administered. The toxicity of the particular vaccine which is going to be administered

has to be considered. Some vaccines can be given in large doses, even in acute cases, without the slightest reaction, whereas with others great care must be taken in feeling one's way, otherwise an alarming reaction may occur. Thus, with *Streptococcus pyogenes* in an acute case it is well to begin with not more than two million cocci, whereas with Bordet's bacillus of whooping cough or with Pfeiffer's bacillus of influenza very large doses can be given even in acute cases with impunity. When the infection is a chronic one, and where even if there be a small flare-up it will not seriously inconvenience the patient—for example in sycosis or furunculosis—the dose should be rapidly increased by successive increments of from 50 to 100 per cent., until there is a very marked improvement or until there is evidence that a slight overdose has been given as shown by an exacerbation of

the local condition or by some fever or malaise after the inoculation; that is, until there is a focal or a general reaction. When there is evidence of this overdose, then the next dose should be reduced to the last one which failed to produce any "reaction," and the subsequent increases should only be gradual. If there is marked improvement before any "reaction" is evident (as is very often the case), then the same dose that produced the improvement should be repeated several times, as evidently something approaching the optimum dose for the particular patient has been found.

Where the infection is a chronic one, but where it is not safe to risk any considerable exacerbation of the condition—for example, chronic bronchitis, the best procedure is to give a safe dose and to increase the dose gradually. A little time may be lost in finding the most suitable dose, but in such a case this is infinitely preferable to the risk of setting up an acute infection.

In acute infections where it is essential that no "reaction" should be induced—for example, bronchopneumonia, erysipelas, etc., it is wise to give very small doses and to repeat them often (every twenty-four or forty-eight hours if necessary). In all cases in which with a certain dose definite improvement is manifested, it is wise to repeat the same dose next time and possibly for several times. If, instead of doing this the practitioner increases the dose according to a definite prearranged scale, then it is quite likely that he will rapidly increase the dose beyond the optimum and undo all the good which he has done with the first dose.

[The importance of these dose rules can hardly be over-emphasized, as upon their intelligent interpretation the success or failure of the treatment frequently depends.—Ed.]

Results of Vaccine Therapy: In incipient infections, when the microbes are exposed to the full effect of the antibacterial substances elaborated as a result of the injection of vaccine, rapid success may be obtained. Where the infection is of old standing and the circulation through the infected focus has become impeded, success will only be obtained after a long series of immunizing doses; while, in cases in which there are

sloughs or collections of pus, success with vaccines will only be obtainable after the sloughs have been removed or the pus has been evacuated by surgical means. When a vaccine is given for prophylactic purposes it is not to be expected that the immunity will be absolute. Even when an individual is highly immune he may receive such a large dose of a virulent organism that infection will result.

When we examine "colds" bacteriologically we find that while some individuals (and these are in the minority) get many "colds" which are always caused by the one microbe, others (the majority) are infected by one microbe at one time and by another at another time. The same is seen in many cases of chronic bronchitis. This varying flora makes the treatment of respiratory conditions more complicated, but it has had one good effect as regards the vaccine treatment by the practitioner, and that is that it has caused the mixed polyvalent vaccines to be introduced. For routine vaccine therapy practice, where many patients have to be dealt with, and where there is not the opportunity of having extensive bacteriologic investigations done on each patient, these polyvalent mixed vaccines have met with very great success.

The mixed stock vaccine (0.2 c.c.) should be given immediately the "cold" is noticed; and, in a certain number of cases, the attack will be aborted. Even when the cold has developed, the vaccine will generally cut short the attack, and especially the last stage, when there is a profuse muco-purulent discharge from the nose without constitutional symptoms. The vaccine also seems to prevent the infection spreading down to the bronchi. With the common cold, however, the chief value of the vaccine is in prophylaxis. In people who are susceptible to colds the anticatarrh vaccine should be given in the autumn in three doses—0.25, 0.50 and 1 c.c.—and during the winter monthly doses of 1 c.c. may be given. It has been common experience that by this means people can be kept free from colds who, without the vaccine, were having one attack after another through the winter.

The bacteriology of bronchitis is roughly the same as that of the common cold, and very often the attack be-

gins with a cold. If the infection is simple, an autogenous vaccine may be made, but usually the mixed stock vaccine does all that is necessary. Doses of from 0.25 to 1 c.c. of the mixed vaccine for colds or of the anticatarrh vaccine are given at intervals of from three to seven days, and after the first one or two doses the patient notices the improvement. The condition usually improves rapidly up to a point at which it gives little trouble to the patient; and, when this stage has been reached, if larger doses are given monthly the infection gradually disappears.

In influenza, Fleming believes that even though the primary cause of the infection is obscure, there is not the slightest doubt that Pfeiffer's bacillus, together with the pneumococcus and streptococcus, are responsible for the complications of the disease, and that it is to them that the bronchopneumonia which caused the mortality was due. Fleming thinks that the best combination is the one which contains 500 million Pfeiffer's bacillus per c.c. with 1,000 million pneumococci and 100 million streptococci. It has been shown that very large doses of the pneumococcus can be given with impunity and that better immunity followed these larger doses than was obtained with the smaller ones. Small doses of one of the anti-influenza or anticatarrh vaccines were of very great benefit in the treatment of bronchitis and bronchopneumonia which followed influenza. Doses of about 0.1 c.c. of the prophylactic vaccine were given immediately and repeated in twenty-four hours if the temperature still remained high.

In the prophylaxis of pneumonia, Lister, who continued Sir Almroth Wright's work in South Africa, ascertained which were the common types of pneumococci causing pneumonia on the Rand, and he prepared a mixed stock vaccine containing all the types, which he administered to the natives in large doses with wonderful effects as regards the prevention of the disease. Whereas the incidence of pneumonia before vaccine therapy was instituted was 70 or more per 1,000, it dropped during the year when Lister was giving his vaccine consisting of mixed types of pneumococci to about 4 per 1,000. The effect on the mortality from the disease was even

more striking, as this dropped from about 20 per 1,000 to 0.86.

As regards the treatment of lobar pneumonia with vaccines, it is much less easy to obtain reliable figures owing to the great variations which are observed normally in the course of the disease. Wright's observation that the disease can be prevented by inoculation during the incubation period shows that large doses of the vaccine can be given with safety and without producing a negative phase and a number of reports have been published showing that the administration of vaccine shortened the disease and hastened the crisis. It must be remembered, however, that when the lung is consolidated there is a very large amount of tissue swarming with pneumococci through which the circulation is greatly impeded, so that even if a certain amount of immunity is produced the immune bodies will have difficulty in obtaining access to the seat of infection. There seems to be no doubt that the administration of vaccine aids the resolution of pneumonia and hastens recovery.

The author is a believer in whooping-cough vaccine, which for the treatment of the disease should be a mixed vaccine. This vaccine is very little toxic, so that even for small children comparatively large doses (1,000 or 2,000 million) can be given; and it is well to repeat the doses every two or three days. He believes that three doses of the vaccine should be given at intervals of a week. In some communities of children whooping cough has been almost wiped out by this means.

Chronic rheumatic conditions, including rheumatoid arthritis, fibrositis, neuritis, sciatica, myositis and similar complaints, all seem to take their origin from some chronic infection, which is usually streptococcic. The site of the infection is usually in the mouth or the intestine, and the streptococcus which is responsible is very different from the *Streptococcus pyogenes*, which is the causative agent in acute septic infections, such as erysipelas or acute septicemia; it is of very much less virulence, so that it may infect a portion of the body for years without causing more than slight inconvenience. A common history of a patient with rheumatoid arthritis is that she has had bad teeth for years, the removal of

which was followed by only temporary improvement, after which the arthritis progressed as before. On examination of such patient's stools, it will in all probability be found that there is an enormous preponderance of streptococci, and more especially of streptococci of the mouth type. Doubtless the infection commenced in the mouth, but some of the streptococci which were being continually swallowed escaped destruction by the gastric juice and bile and established themselves in the intestine, where they had continued to flourish. The effect in such cases of the administration of vaccines, either autogenous or stock, has been that in almost all there is some alleviation of the condition, and in some there is apparently complete disappearance of the disease. Owing to the multiplicity of types of streptococci in the mouth and intestine it is frequently better to commence treatment with a mixed stock vaccine which contains a very large number of strains of streptococci from rheumatic patients, and only to proceed with an autogenous vaccine if the stock vaccine fails.

Diphtheria carriers may be freed from bacilli by the administration of a vaccine in a very much shorter time than by any other means. Out of a series of fifty consecutive and unselected patients who received the vaccine in doses of 10 to 60 millions every four days, forty-four were free from bacilli after three doses, and all were free after eight doses of the vaccine.

Attention must be directed to the fact that patients may be inoculated with bacterial products not only from without, but also introduced into their circulation by some disturbance of the infected focus. It does not matter what form the disturbance takes—whether exercise, massage, forcible movements or the active hyperemia induced by the application of a fomentation—the result is the same, the only difference being that, whereas the light forms of disturbance reproduce the effect of a small dose of vaccine, the more severe disturbances may be followed by the same events which follow a large dose of vaccine, a severe “general reaction”—namely, malaise, fever, or even collapse. It follows from this that in the treatment of any patient by vaccines a satisfactory conclusion is only to be arrived at if this phenomenon of

auto-inoculation is considered, and in most cases it is necessary that these auto-inoculations should be diminished or abolished by keeping the infected part as much as possible at rest by splinting or some other means.

The Pertussis Vaccine Question. The pessimistic conclusions of W. C. Davison published in the series on Biologic Therapy in the *Journal of the American Medical Association*, Jan. 22, 1921, and abstracted in the *Practical Medicine Series*, 1920, Vol. VI, page 126, gave rise to objections by Paul W. Van Meter and by Paul Luttinger.⁶ The latter states that failures to obtain results with pertussis vaccine are due to (1) old, inert vaccines; (2) to intramuscular, instead of subcutaneous administration, and (3) insufficient dosage. To this, W. C. Davison to whom these remarks were referred for discussion, adds a fourth and a fifth reason in regard to the therapeutic results of possibly more weight than the preceding three, namely: (4) a careful study of a sufficiently large number of uninoculated pertussis patients as controls, and (5) the realization that equally as enthusiastic and presumably equally as reliable reports are published in favor of the treatment of pertussis with benzyl benzoate, with local applications of resorcin, by a change of air, and with injections of *B. influenzae* vaccines, of ether, of the sterile ether extract of the sputum of whooping-cough patients, and of sugar solutions.

R. K. Ruvalc⁷ is an advocate of the use of pertussis vaccine, consisting only of killed Bordet-Gengou bacilli, in the treatment of whooping cough. His experience covers 130 cases extending over a period of seven years: in six cases the treatment was an absolute failure; in forty-five cases benefit of more or less degree was obtained; seventy-nine cases showed marked improvement, and, in some, results were little short of marvelous. He regards the cases with a complete cessation of symptoms inside of four weeks as being greatly benefited.

Dosage for Infants: An initial dose of from 250,000-000 to 500,000,000 was given, which was increased to 1,000,000,000 or more as the symptoms demanded. From three to eight doses were given at intervals of from

(6) Jour. Amer. Med. Ass'n., Feb. 12, 1921.

(7) Penn. Med. Jour., March, 1921.

forty-eight to seventy-two hours. More than eight doses were unnecessary.

In Older Children: An initial dose of 500,000,000 was given and each succeeding dose was doubled as deemed necessary. Occasionally a reaction was noted by a temporary rise in temperature or increase in the paroxysms. No reaction lasted over twenty-four hours.

The author knows no contraindications, as these vaccines do no harm. He considers this the most valuable treatment known at the present time, though no definite promise of a rapid cure can be given. The vaccine must be used early, preferably during the first or second week to do maximum amount of good, in large doses and at short intervals. Fresh unmixed vaccine should be employed.

Tuberculin Percutaneously in Tuberculosis. That the disappointments experienced in tuberculin therapy of lupus are due to excessive dosage is the opinion of Engwer.¹ He is in favor of percutaneous inoculation of tuberculin, which causes the chief reactions to occur at the point of inoculation, whereby the diseased portion is protected against excessive action while it benefits from the curative influence. This method, which was developed by Ponndorf, consists in the inoculation of two fields on the anterior aspect of the thigh and the outer surface of the arms. After cleansing and disinfection of the part with ether, thirteen or fifteen superficial incisions 2.5 cm. (one inch) long are applied closely together, which are then crossed by others placed at right angles to these. A considerable amount of bleeding should be prevented by using a v. Pirquet lance or the blunt end of a scalpel. Into this field, one or two loopfuls of old tuberculin are rubbed. In young individuals generally at the beginning of the treatment it is best to employ the remedy in 50 per cent. dilution. After drying, dressing is not required if the patient wears clean clothes. The reaction may vary from erythema and edema to vesicles, pustules, and even ulceration and necrosis. The severe reactions are only likely to occur in youthful individuals with undiluted tuberculin.

Febrile reactions occur rarely and are not desirable.

(1) Therap. Halbmonatsh., May 1, 1921.

Focal reactions commonly occur causing an increase in discharge and the affected area to become redder, more swollen and painful.

The treatment may be repeated every two or four weeks when traces of the previous application have disappeared, and continued for many months according to the nature of the case.

The best results were obtained in scrofulous dermatitis and in suppurative tuberculosis of the lymph glands in which latter condition the best results are obtained by a combination of tuberculin and roentgenotherapy. Less favorable are results in lupus vulgaris, in which the hypertrophic ulcerative forms only are benefitted, while the dry flat form resists further treatment.

H. Koopmann² advises the use of dilute tuberculin for inoculations, commencing with 1 per cent. and increasing progressively to 10, 25 and 50 per cent. With this modification excellent results are obtained, he says, without danger of uncontrollable reactions.

Desensitization in Asthma and Hay-Fever. In contrast to the results obtained in testing and treating typical hay-fever patients against pollens, A. H. W. Caulfield³ points out that comparative disappointment will be experienced in this respect in cases of bronchial asthma, due to the fact that bronchial asthma is a syndrome which may have widely different etiologic agents. It will frequently be found as a complication of, or augmented by, other pathologic lesions, and it may by itself be accompanied by a variety of complications, such as those induced by repeated attacks of true bronchopneumonia. The greatest difficulty has been experienced in distinguishing between chronic bronchitis with exacerbations and the varied types of dyspnea incident to this condition, and true bronchial asthma with an added bronchitis.

From the standpoint of sensitization, this distinction may not be so essential, if one regards bacteria as capable of causing the syndrome of bronchial asthma by inducing sensitization in a manner comparable to the phenomenon as incited by the epidermal proteins. This

(2) Münch. med. Wochenschr., 1921, p. 205.

(3) Jour. Amer. Med. Ass'n., April 16, 1921.

conception is based on the theoretical grounds and clinical evidence that bronchial asthma may disappear after the removal or successful treatment of areas harboring foci of infection. However, the results of autogenous vaccine treatment of bronchial asthma can not be compared to the much more satisfactory results obtained in cases in which specific proteins can be used. Furthermore, positive skin reactions with bacteria have been obtained so rarely that, as a routine, this test has practically been discarded. One is inclined to try autogenous vaccines in those cases in which we fail to demonstrate protein sensitization, and for which, after full and careful clinical examination, including the examination by a nose and throat specialist, we can find no definite reason for the bronchial asthmatic symptoms. The failure of vaccine, in contrast to protein therapy, is sufficiently marked to cause one to question that both are etiologic agents, acting in a comparable fashion.

Of 161 cases of bronchial asthma and perennial hay-fever which had been tested for sensitization by the cutaneous tests, forty-seven or 29 per cent. gave positive skin reactions. This agrees well with Sanford's results of 25 per cent. The following figures indicate the frequency with which positive reactions were obtained to the various proteins: horse dander, 20; dog hair, 17; cat hair, 15; rabbit hair, 1; goose feather, 1; chicken feather, 11; horse serum, 6; rabbit serum, 1; egg, 5; casein, 4; milk, 3; beef, 2; lamb, 1; salmon, 1; barley, 3; oat, 11; wheat, 6; rye, 7; corn, 5; potatoe, 1; buckwheat, 2; bean, 3; rice, 1; celery, 2; tomato, 2; banana, 1; Brazil nut, 1; cheese, 1; tobacco, 1; and *Staphylococcus albus*, 1. It will be noted that outstanding in frequency and importance, are the epidermal proteins.

The previous history of asthma in childhood or early youth is a very valuable indication regarding the probability of protein sensitization.

Technique of the Tests: Sets of four or five cuts are made with a scalpel on the cleansed flexor surface of the arm, of such a depth that only the minutest droplet of blood appears. With a Wright pipet and teat, a drop of 0.4 per cent. potassium hydroxide or sodium hydroxide is deposited on each cut. A glass spatula is dipped into

the dried protein or pollen and rubbed into the cut, a separate spatula being used for each protein. A positive reaction shows up in from five to fifteen minutes, or sooner, as a clear cut wheal surrounded by an areola of hyperemia. Frequently the reaction will begin to subside in from ten to fifteen minutes, although in this there is considerable variation. The degree of the sensitization is estimated by measurement of the wheal. Especially if this is large it is often somewhat irregular. The distinctions the author would make between a true and a spurious reaction are that the borders of the latter are less clearly defined, they seldom measure from 4 to 5 mm. in diameter, and they usually appear singly or in groups that are not in harmony with the indications in the particular case.

Treatment: When the offending protein can not be deleted from the patient's food or removed from his environment, injection with protein solutions is at present the best means we have to induce desensitization. However, the majority of patients need repeated courses of injections continued over long periods of time, if they are to be kept protected against the etiologic agents. Desensitization is best accomplished by observing the following rules:

(a) The increase of dose ideally should be such as to produce a local reaction approximating the threshold of a slight general reaction.

(b) The interval should be as short as possible and reinjection given at or about the time the local reaction completely subsides. Practically, this will vary with these injections between two and four days.

(c) The dose should be increased as much as possible, confoming to (a) and never decreased.

Hay-fever tests made with the dry pollen almost invariably gave larger reactions than were obtained with the commercial solutions. Major reactions were obtained against the following pollens, and treatment was given against most, if not all: alder, sweet vernal, meadow fox tail, orchard grass, June grass, timothy, red top, daisy, dandelion, plantain, yarrow, mustard, golden glow, dock, rye, corn, sunflower, dahlia, cosmos, golden-rod, and ragweed. There are pollen positive cases with-

out clinical manifestations. These are well illustrated by the results obtained with the daisy pollen. This pollen was used as a test in sixty-five cases, major reactions being obtained against it in twenty-two instances, and positive (lesser) reactions in twenty-three. The daisy pollenates here in June and July, but, in none of these cases were there clinical manifestations of hay-fever during this period, unless there was also sensitization to other pollens of the early summer type.

[It is interesting to compare the rules laid down for desensitization against proteins in the preceding abstract with the principles of vaccine therapy given, *e. g.*, by Alexander Fleming (p. 110). It is but rational to assume that we may proceed more boldly against a dead poison, such as a toxic protein, than against a living virus.—ED.]

Serum Desensitization. George H. MacKenzie⁴ presents the following classification of individuals hypersensitive to horse serum :

1. Spontaneously hypersensitive.
 - A. "Horse" asthmatics.
 - (a) Cutaneous reactions positive to both horse dander proteins and horse serum.
 - (b) Cutaneous reactions positive to horse dander proteins, but negative to horse serum.
 - B. Individuals with no history of asthma or previous serum treatment, but with a cutaneous reaction positive to horse serum.
2. Artificially sensitized.
 - A. Those to whom serum has been administered intraspinaly.
 - B. Those to whom serum has been administered intravenously or into the tissues.

In this classification, an effort has been made to arrange the group in the order of decreasing hypersensitiveness. While abundant clinical evidence indicates that many patients do not become hypersensitive after serum treatment, and in many others the hypersensitiveness is short lived, and, when it does persist for years, it is often a low grade of hypersensitiveness, there is unquestionably a small group who remain for one or two years, or perhaps longer, after a serum treatment, in a condition which demands great caution when serum

has to be administered a second time. This applies particularly to those who have been given serum intravenously or intraspinaly. Despite a few exceptions, the hypersensitiveness will be found to decrease from above downward as the several types are arranged in the foregoing classification. It is with patients in Group 1 that the utmost caution must be exercised. Some of the so-called "horse" asthmatics are so exquisitely hypersensitive that even minute amounts may prove fatal. Most, but not all, of the fatal serum accidents on record have occurred in this type of patient. Some, however, come from Group 2. What, then, is to be done when one of these hypersensitive patients has diphtheria, tetanus, a Type I pneumococcus infection, meningococcus meningitis or bacillary dysentery? It is commonly stated that a desensitizing dose of 0.5 or 1 c.c. should be given subcutaneously before the whole quantity of serum is administered. In some cases this may suffice; but in many cases such a procedure is entirely inadequate. Besredka introduced a method which consists of giving intravenously at intervals of from two to ten minutes increasing doses of serum, beginning with 1 c.c. of a 1:7 dilution. This forms the basis of the methods which, so far as is known, offer the best hope of desensitization. Experience has demonstrated beyond question that, before serum is administered, information regarding the presence or absence of hypersensitiveness should be obtained. One should find out whether the patient has had asthma or allergic rhinitis from horses, or whether he has previously been treated with serum, and if so, by what route the serum was administered. An intracutaneous test should be made with horse serum in 1:10 dilution, injecting 0.1 c.c. or less—preferably 0.02 c.c. A control test with physiologic sodium chloride solution or better, with a 1:10 dilution of rabbit or sheep serum, should be made at the same time. One should wait half an hour before deciding whether the reaction is positive or negative. The interpretation of the mild type of positive reaction is not always easy; but if there is a definite enlargement of the small elevation caused by injecting the serum into the skin, and if this injection wheal is surrounded by a zone of erythema, the test is positive;

provided the control test has not behaved in a similar way. The size of the wheal and its surrounding zone of erythema give a rough index of the degree of hypersensitiveness. There are, however, a few patients in whom the skin test fails to reveal a state of hypersensitiveness.

If the patient has had asthma and gives a positive skin test, great caution is necessary. The first desensitizing dose should be given subcutaneously, beginning with a dose not larger than 0.025 c.c. The dose should be doubled every half hour until 1 c.c. is given. Then 0.1 c.c. is given intravenously. After twenty minutes the dose is doubled. In case the therapeutic serum is to be given intravenously, the intravenous injections are continued, the dose being doubled every twenty minutes until 25 c.c. have been given without reaction. Four hours later, 50 c.c. may be given, and after eight hours the treatment may be continued in the usual manner. In case a reaction occurs, one should wait the usual interval, and then the last dose that gave no reaction or only a mild one is repeated. There is no evidence suggesting a cumulative action. The first portion of the serum should always be given very slowly and careful watch kept for respiratory embarrassment, cyanosis, skin eruptions, edema and symptoms of collapse.

In case the therapeutic serum is to be administered intraspinally, the subcutaneous doses should be carried out in the same way and four or five of the intravenous doses given, when, if there has been no reaction, the intraspinal route should be tried very cautiously. It should be realized, however, that in the exquisitely hypersensitive patients with bronchial asthma, serum therapy may be impossible.

It is probably quite safe with some of the less sensitive patients to shorten the desensitization program in case the first few injections produce no reaction. This may be done by increasing the doses a little more rapidly than by doubling the preceding amount. The first intravenous dose should, however, never be more than one-tenth of the largest dose tolerated subcutaneously. Finally, when attempting desensitization, one should never inject serum without having epinephrine at hand.

(B) NON-SPECIFIC ANTIGEN THERAPY

Proteotherapy. The general principles and uses of proteotherapy are well discussed by Paul Kaznelson.⁵ This method of treatment, which has been advocated in so many conditions that it might almost seem a panacea, depends upon increasing the functional activity of living protoplasm. If the organism has no weapon against a certain harm, then proteotherapy can have no effect. It can merely increase the degree to which the available means of defense are used. It does not bring into action new defensive measures, as does the more powerful chemotherapy. Another limitation of proteotherapy is the fact that only certain doses increase the protoplasmic function. A slightly larger dose produces the very opposite of the result desired, namely, a diminution in the function. Even the effective dose will cause a temporary diminution of defensive activity—the negative phase. Furthermore, there is no definite dosage for any one protein; but it varies considerably from one case to another, according to congenital predisposition or constitutional modification acquired by disease. Proteotherapy is decidedly a two-edged sword. The principle of dosage, therefore, in all cases, is to begin with small doses; and, when these produce no result, to increase the quantity slowly according to the evolution of the excitation in the particular individual.

The fear of inducing anaphylaxis is entirely unjustified. None of the proteins employed, with the exception of serum, are capable of producing true anaphylaxis in man. By giving the injections at sufficiently short intervals, that is, during the anti-anaphylactic stage, this reaction can be avoided. Thus the author uses milk injections at intervals of two days. When giving milk injections intramuscularly, it is extremely important to avoid intravenous injection; hence, the piston of the syringe should always be pulled upon before injecting to see whether blood enters the syringe. Definitely associated with these injections is the frequent occurrence of fever, preceded by chill, and not infrequently accompanied by nausea, headache, and pain at the point of

(5) Therap. Halbmonatsh., May 1, 1921.

injection. In addition, a focal reaction frequently occurs, that is, a temporary aggravation of the condition for which treatment is given, due to the establishment of a negative phase. Abscesses at the point of injection never occur, when proper asepsis has been used.

The number of proteins that have or may be employed is enormous. For certain conditions certain special proteins are preferred, probably chiefly for historical reasons rather than because of necessity. Thus, the various bacterial preparations probably owe their therapeutic action in a large measure to non-specific response, even in homologous diseases. Next in order of frequency in use may be mentioned the various sera, such as normal serum of animals, autoserum, convalescent's serum, exudate, and even blood. An animal product which, especially of late, has enjoyed extensive use, is the injection of milk⁶ first introduced by R. Schmidt, and Saxl. Ordinary cow's milk sterilized by boiling is injected into the gluteal muscles in an average dose of 5 c.c. except when unusual susceptibility is suspected, as in tuberculous patients. Often a dose of 5 c.c. is incapable of exciting a reaction and the dose has to be increased to 7, 10 c.c. and even more. The inquiry regarding the active principles of milk has led to the isolation of casein and its preparation for intravenous injection, in the form of such preparations as "Caseosan," in ampules. This brings us to the simple chemical bodies that have been used for this purpose, oldest among which is nuclein, which was employed for the purpose of increasing the number of leukocytes. Its place has been taken by various albumoses, of which, "deuteroalbumose" is perhaps the most generally employed (dose—1 c.c. of 10 per cent. solution increased daily by 0.5 c.c.). To this must be added, because of very similar mode of action, the injection of colloidal metals, the production of fixation abscesses, *e. g.*, by turpentine, and finally a certain portion of the effect of certain so-called organotherapy.

Indications. Infections give the chief indication for proteotherapy, especially those that are torpid and have

(6) Details of technique are given in Practical Medicine Series, 1920, Vol. VI, p. 136.

a tendency to chronicity. Heart weakness, hemorrhages, and grave cerebral disturbances require great caution in initial dosage. In typhus, dysentery, and scarlet fever, intravenous injection of from 40 to 60 c.c. of convalescent serum or normal human serum is indicated, providing the treatment can be given within the first three days, and the case shows a severe tendency. In mild cases, this treatment is not required. In influenza, the injection of almost any variety of serum seems to have given favorable results in certain cases. The same may be said of milk injections. In erysipelas, milk injections have often produced a favorable end with crisis.

The use of proteotherapy is indicated in all kinds of chronic and sub-acute arthritides, though it takes great patience and often many injections to produce satisfactory results. Established deformity and ankyloses are not influenced. When a certain amount of improvement has been secured, further continuation of the injections is often without benefit.

In other gonorrheal complications besides arthritis, such as epididymitis, prostatitis, and buboes, also in soft chancre, milk injections have been found valuable. Female gonorrheal inflammation of the adnexa is not so favorably influenced, possibly because the stimulus is too feeble. It may take intravenous administration.

This method may also have diagnostic value. Thus it may be employed as a provocative measure in latent gonorrhea, as gonococci might be demonstrated after milk injections when they were absent previously. In tuberculosis a hypersusceptibility exists not only to tuberculin, but also to proteotherapy, so that milk injections in very small doses will produce a reaction analogous to tuberculin.

From what has just been said it will be seen that proteotherapy must be used in tuberculosis with great caution, as to dosage. For instance, an initial dose of 0.1 c.c. of milk may have to be used to be followed in two or three days, in case there be no reaction, by dosage increased by 0.1 c.c., etc.

Dosage in Proteotherapy. F. Kleeblatt⁷ advises the use of small doses, so as to avoid stormy clinical reac-

(7) Therap. d. Gegenw., June, 1921.

tions, as these are not at all required for good results. The aim should be to produce gentle reactions such as might at times only be detected by blood examination. He has frequently found an intramuscular injection of from 0.1 to 0.3 c.c. of milk sufficient to produce a satisfactory therapeutic result. If no reaction is obtained, the dose is gradually increased until a dose is found that produces either a local, focal, or general reaction; and another dose must not be given until all the reactions of the previous injection have disappeared.

The author advocates making use of a differential leukocyte count for the purpose of studying the reaction. He takes a blood smear before the injection, another, if possible, six hours later, and then others after two and four days. In general, the reaction has subsided by the fifth day. Once the reaction of the individual has been ascertained it is not necessary to repeat the blood examination on repetition of the same dose, which it is advisable to continue until the result has become slight or *nil*; then it is desirable to renew the blood examinations together with an increase in dosage. The most marked change in the blood is usually found in connection with the number of lymphocytes.

The chief use for such treatment Kleeblatt finds in torpor of inflammation, that is, in cases in which this great healing reaction of Nature is not intense enough to produce a cure. An advantage of this therapy is that it may bring to light latent foci, which may require special local treatment. Kleeblatt advises caution in case of eosinophilia. He considers exudative diathesis and helminthiasis, contraindications.

Caseosan. To overcome the disadvantages of milk injections dependent upon the variation and composition of cow's milk, its painfulness on subcutaneous or intramuscular injection, and the frequently severe reactions, attempts have been made to supply the pure active principle which was found to be the milk proteins. A preparation of these has been introduced in Germany under the name of "Caseosan" obtainable in ampules and suitable for intravenous injection.

Hans Förster¹ employed this preparation in twenty-

(1) Therap. Halbmonatsh., April 1, 1921.

seven patients suffering from buboes with the result that fifteen of the buboes that had become very soft were absorbed without requiring incision, six other extremely soft buboes either ruptured spontaneously or were incised. Four buboes that were not yet soft at the beginning of the treatment rapidly softened and then healed. The healing of two buboes that had perforated, before treatment was commenced, was decidedly accelerated.

Injections were given intravenously on alternate days in ascending dosage, the first day 1 c.c., the third day 2 c.c., and the fifth day 5 c.c. and this sequence was repeated until decided improvement occurred. It required an average of from four to six injections, but in some cases as many as fifteen. Disagreeable effects, aside from rise in temperature with chill and malaise, have not been noted. On the other hand, patients were unanimous in declaring that pain and tension in the inflamed bubo were relieved immediately after the first injection, and the febrile reactions were preferred by them to the necessity of incision.

Caseosan in Obstetrics and Gynecology. R. T. von Jaschke² reports favorable results from proteotherapy in puerperal infections, as well as in parametritis of other causation, torpid swellings of the adnexa, and genital and peritoneal tuberculosis. He also believes that something can be accomplished by this therapy in connection with operation or radiotherapy in carcinoma.

The mode of action of this form of treatment the author believes to be due to increased antibody formation rather than to leukocytosis, for the latter is not always present even in cases that react favorably. On the other hand, it has been found possible by means of a technique elaborated by Salmon³ to prove the formation of specific antibodies by means of precipitation and complement-fixation reactions, which it is hoped might develop into a means of estimating the indications for, as well as efficiency of, this form of treatment.

v. Jaschke who used caseosan finds that patients whose serum contained casein antibodies prior to the injection, give severe general reactions to these injections; hence,

(2) *Therap. Halbmonatsh.*, Sept. 1, 1921.

(3) *Münch. med. Wochenschr.*, 1920, No. 52.

in such cases, the first injection should be given intramuscularly and according to the degree of antibody titer in doses of 0.1 to 0.5 c.c., which should not be repeated until after three or five days. If, on the other hand, there is but little of casein antibody in the patient's serum, the first dose may safely be 0.5 c.c. given intravenously and followed in two days by a 1 c.c. dose. Subsequent injections should be preceded by an estimation of the amount of antibody. If this increase slowly, the injections may be given intravenously. If, however, the antibody titer increase rapidly, subsequent injections should be given intramuscularly and in small doses. In acute infections the number of injections is determined by the severity of the process of the individual reaction. In other conditions, patients usually receive a series of three or four injections followed by another series after an interval of six or seven days.

In cases with an initial small amount of antibody, caseosan has been found much more effective than in those cases in which the normal serum contained a large amount of casein antibody. Best results can only be expected from the early use of these injections. In the presence of septicemia the treatment is usually too late.

ANTIBODY THERAPY

Immune Serum in Scarlet Fever. G. H. Weaver⁴ has come to look upon injections of serum of convalescent patients as a valuable agent in the treatment of scarlet fever. He usually injects the serum intramuscularly in amounts of from 60 to 90 c.c. Often one-half is injected in the muscular mass on the outer side of each thigh. Occasionally it has been injected intravenously, but with no apparent advantage. A second dose after twenty-four hours has been given at times when the first dose was not followed by satisfactory improvement, or when improvement was followed by tendency to relapse to the previous condition. The most prominent beneficial effect from injections is the improvement in the general condition of the patient, which is out of proportion to the

(4) Jour. Amer. Med. Ass'n., Oct. 29, 1921.

alteration in the temperature curve. Two or three hours after the injection the temperature begins to decline and continues to do so for from twenty to thirty-six hours. It sometimes reaches normal, but usually remains a little above. Subsequently, there is usually a moderate rise followed by a gradual fall to normal. Occasionally the fever terminates by crisis, never again rising above normal. The earlier in the disease the serum is given, the more pronounced is the effect on the temperature. Figure 19 represents the composite temperature curve in

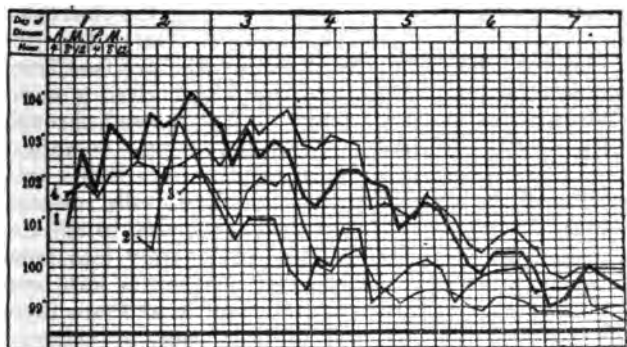


Fig. 19. Composite temperature curves: 1, twenty patients receiving no serum; 2, four patients receiving serum on the second day; 3, ten patients receiving serum on the third day; 4, twenty-five patients receiving serum on the fourth day.

cases in which serum was given on the second, third, and fourth days, and in a series of twenty in which no serum was given. The latter cases were of the same type as treated cases and occurred in the hospital during the three years before serum was used. It was noted that, when serum was given on the second and third days, the initial drop of temperature was marked, with little subsequent rise. When serum was given on the fourth day, the curve did not differ materially from that of the controls. However, many cases in which injection was made on the fourth day showed a pronounced drop in temperature, which did not appear on the composite curve because of the modifying influence of septic

complications in many of the cases. When serum is given in acute cases, with septic complications, an initial fall in the temperature with improvement in the general condition usually occurs, but the temperature again rises and the complications run the usual course. Two or three hours after the injection delirium and restlessness begin to subside, the pulse improves in quality and is slower, cyanosis disappears, and a patient who had appeared to be on the brink of dissolution in the afternoon when the serum was given appears well on the road to recovery the next morning.

Technique: The blood is drawn during the fourth or early in the fifth week of the disease. Only those individuals are used as donors of serum who are free from all suspicion of tuberculosis, whose blood gives a negative Wassermann reaction, and who have passed through a typical scarlet fever attack without septic complications. The blood is drawn, with aseptic precautions, into a sterile bottle holding 500 c.c., through a needle inserted into a vein at the bend of the elbow, from 200 to 300 c.c. being taken from adults and proportionately less from the larger of the children. After the serum has been separated from the clot, it is drawn off, that from three or four patients mixed, and 0.3 per cent. of tricresol added. Cultures are made from the mixture. If it proves sterile, it is placed in small bottles of 30 c.c. capacity, cultures are again made for sterility, and the bottles are tightly corked and paraffined and kept in a refrigerator until used. Serums have usually been used within a few weeks. In a few instances, serums several months old have been used, but apparently they were less effective than fresher ones.

Intramuscular injections of citrated blood, as recommended by Zingher, may be employed anywhere. When scarlet fever is prevalent, convalescents are usually available, and freshly drawn blood may be injected when facilities for obtaining and preserving serum are absent. This makes the procedure practical in private practice and especially in large hospitals for contagious diseases, in which suitable convalescents are always available. Several advocates of serum treatment for scarlet fever report some value in normal serum, but less than in

serum from convalescents. Hence, in the absence of available convalescent serum, normal blood may be used.

Specific Serum Therapy of Yellow Fever. H. Noguchi¹ reports that anti-icteroides serum reduces the mortality in yellow fever when used on or before the third day of the disease. Of 170 cases, ninety-five have been treated on or before the third day, with thirteen deaths (13.6 per cent. mortality), while the average death rate of untreated patients during these epidemics has been 56.4 per cent. (442 deaths among 783 cases not treated with serum). On the other hand, treatment with serum after the fourth day has no appreciable effect, since there were thirty-nine deaths among the seventy-five cases (52 per cent. mortality).

Prophylactic inoculation by means of the injection of 2 c.c. of the killed culture of *Leptospira icteroides* (containing at least 2,000,000,000 organisms per cubic centimeter) is of definite protective value. Among 3,230 persons vaccinated twice, no case of yellow fever developed, while 278 cases occurred among the non-vaccinated notwithstanding the fact that both groups of individuals were equally exposed to infection. Among 4,307 persons receiving only a single inoculation of the vaccine, only five suspicious cases developed. The protection does not become effective until about ten days after the last injection.

FUNCTIONAL THERAPY

CATHARTICS

Dosage of Cascara Sagrada. Hugh McGuigan² finds, as a result of experiments on himself and students, that cascara sagrada should never be used as a cathartic but only as a laxative. When more than 2 c.c. is needed, some other drug should be used. A dose of 2 c.c. will cause two movements of the bowels in from five to twelve hours. There is usually considerable griping from this dose, which begins in about four hours and may last

(1) Jour. Amer. Med. Ass'n., July 16, 1921.
 (2) Ibid., Feb. 19, 1921.

twenty-four hours. When 4 c.c. are used, abdominal tenderness, griping, and other abdominal symptoms appear which indicate a congested or inflammatory condition of the bowel. If from 20 to 60 c.c. are given to a dog the drug produces excessive diarrhea, often vomiting, and an inflammatory condition of the whole gastrointestinal tract.

Use of Agar in Facilitating the Removal of a Swallowed Foreign Object. LeRoy S. Weatherby³ suggests the use of agar in addition to the eating of as much bulk-forming food as possible, such as shredded wheat, oatmeal, bread and milk, potatoes, carrots, spinach, and celery. Since agar is not digested and swells to several times its bulk, it not only hastens peristalsis, but its added bulk assists in encasing the object and in carrying it along. This effect would be of special value in those portions of the digestive tract in which the digestible food is in the state of emulsification. He advises the addition of three or more heaping teaspoonfuls of chocolate-coated granular agar to a little prepared cereal.

Phenolphthalein Dermatitis. Samuel Ayers⁴ reports six cases gathered from literature and adds a new case. In four of the seven cases the eruption was a sort of erythema perstans in which wheal-like lesions of a pink, yellow, or gray appeared rather suddenly and persisted unchanged for weeks or months, usually disappearing soon after the administration of phenolphthalein was stopped. Itching was frequently annoying. No systemic symptoms have been reported.

CARMINATIVES

Effect of Dilute Solutions of Volatile Acids on Intestinal Movements. The effect of volatile oils in the form of the official "waters," that is, saturated aqueous solutions filtered clear by the use of talcum, has been studied by O. H. Plant.⁵ These were injected either undiluted, or after dilution with several volumes of

(3) Science, Sept. 9, 1921.

(4) Jour. Amer. Med. Ass'n., Nov. 26, 1921.

(5) Jour. Pharm. and Exper. Therap., November, 1920.

water, into dogs with Thiry-Vella loops. Sometimes the solution was diluted spirit of volatile oil; that is a 10 per cent. solution in alcohol, diluted with from 5 to 20 volumes of water. The effect observed was in every case to increase the muscular movements, both in tone and rhythmic contractions. These effects are lessened but not abolished by atropine. They are abolished when the sensory nerve endings of the muscles are paralyzed by cocaine (Fig. 20).

“While the experiments were not of a character that enables one to state these differences quantitatively, it is possible from the results obtained to arrange the oils roughly into two groups, which merge more or less into each other: thus, the *stronger* oils produce a pronounced effect in dilute solution, the *weaker* ones show less effect and require stronger solutions to bring it about. In the former group would be included the volatile oils of mustard, cinnamon, peppermint, cloves, nutmeg, spearmint, juniper and lavender, as well as menthol and camphor; in the latter the oils of anise, cardamon, fennel, orange, and caraway.”

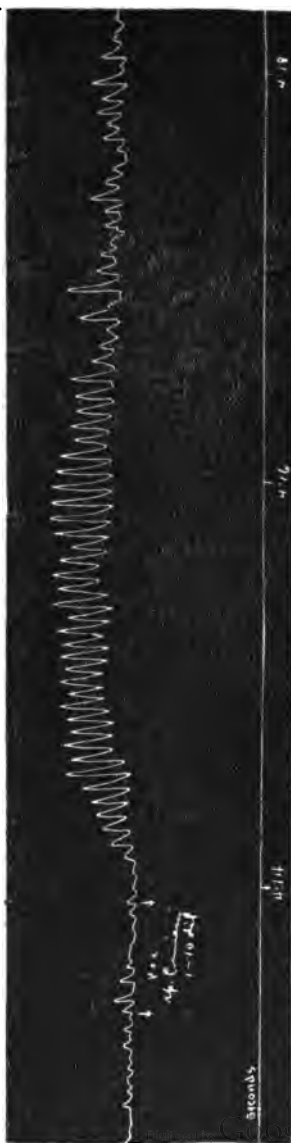


Fig. 20. Dog "G" Balloon filled with air. Small bellows recorder. Fast drum. 8 c.c. of spirit of cinnamon, diluted 1:10, introduced into the loop between the arrows.

ANTISPASMODICS

Possible Dangers of Benzyl Benzoate Therapy. Ludwig A. Emge⁵ warns us to look for harmful possibilities of benzyl benzoate, which so suddenly has grown popular as an antispasmodic on the basis of Macht's experiments. Certain animals can resist greater amounts of this drug than others. For instance, herbivorous animals will fare better than carnivorous animals, because the former have the faculty of metabolizing benzyl compounds much more rapidly, converting them into hippuric acid. Most of our experimental work of today is done on rabbits; and, since they have this faculty, we must be careful in our conclusions as to dosage for man, and not consider ourselves safe when we use proportionately smaller doses.

Macht's study was challenged last year, when Mason and Pieck found that in dogs it would take a very much larger dose than previously reported to obtain antispasmodic effects. In fact, if they succeeded at all in relieving such conditions as an artificially produced pylorospasm, the animal would die from respiratory paralysis. Mason and Pieck were doubtful as to the antispasmodic action in the intestine, spleen, kidney, and uterus, because such very large doses were needed to obtain only a slight relaxation of the smooth musculature. Their failure to demonstrate bronchial dilatation, even after very large doses, is quite significant. Mason and Pieck were impressed with the marked depressing effect on the respiratory center as well as the marked fall in blood-pressure. It is interesting that they noted a weakening action on the myocardium, which Macht had denied.

When Emge began to use it in carefully selected cases of spasmodic dysmenorrhea, the results were variable, and really spasmodic dysmenorrheas are rare. Various preparations were found to vary distinctly in their potency. Twenty per cent. alcoholic solutions were found to deteriorate rapidly, and for this reason the pure substance was given in hermetically closed capsules. Ten-minim doses were used three times a day,

(5) Calif. State Med. Jour., September, 1921. Digitized by Google

for a period of approximately eight to ten days overlapping the menstrual period. Late in 1919, when treating this form of dysmenorrhea, he observed in two young women the recurrence of an appendicitis, which had been dormant for many years. In both of these patients the blood count bordered on a leukopenia, contrary to what we usually see in a "flare-up" of an old appendicitis. Within a few weeks a colleague reported a similar observation with the same blood findings. This led to an investigation of the effect of benzyl benzoate on the leukocyte count and on antibody formation. From his results the author concludes that benzyl benzoate has a definite influence on the composition of the blood picture in the rabbit. It also seemed to favor the recrudescence of latent or quiescent infections. By experiments on antibody formation, by immunizing rabbits with goat's blood, it was found that benzyl benzoate has a depressing influence on the formation of hemolysins in rabbits. Coupling this finding to previous observations, the author feels justified in saying that this substance has a depressing influence on other antibody formations in the rabbit.

Observations on the influence of benzyl benzoate on the blood picture in women in fifty or more cases gave results so variable that a definite opinion can not be given until more material has been collected. Emge is under the impression that very small doses, such as 5 minims three times a day for a few days, have no other effect, than to raise the number of lymphocytes slightly. Where 10-minim doses were given three times a day over a similar period, he has seen repeatedly mild leukocytosis followed by a drop below normal, with the same shifting in the differential count as observed in smaller doses.

The author expresses doubt as to the actual value of benzyl benzoate as an antispasmodic, when it is used in small doses. If larger doses will be needed in order to produce an antispasmodic action, we must consider the experimental proof that this substance paralyzes the respiratory center, lowers the blood-pressure, weakens the myocardium, influences the blood-forming mechanism, and depresses antibody formation to a degree which

allows latent infections to become active. Until further proof is forthcoming that these results obtained on animals are wrong, or that we do not have to fear such results in man, we must select our patients for benzyl benzoate therapy with all these possibilities in mind, and keep our dosage within very narrow limits in order to avoid unforeseen disasters.

[I have not been able to obtain benefit from benzyl benzoate, in the usual doses, in quite a number of cases in which one might have expected relief according to the claims made for it.—Ed.]

Benzyl Cinnamate. C. Nielsen and J. A. Higgins⁶ found that benzyl cinnamate has a more powerful relaxing influence on intestinal musculature than has benzyl benzoate on intravenous administration of acacia emulsion. Benzyl cinnamate is a solid substance at ordinary temperature, which readily melts at the temperature of the body. It seems to be virtually non-toxic on oral administration. The authors have fed $\frac{1}{2}$ oz. to a 10 lb. dog without noticeable symptoms.

[This last observation forces one to doubt whether this substance is sufficiently absorbed on oral administration to have any value whatever; and intravenous administration of acacia emulsion is, of course, practically out of the question.—Ed.]

ECBOLICS

Quinine as Ecboic in Treatment of Abortion. Quinine is advocated by K. Seggelke⁷ in the treatment of abortion complicated with prolonged and excessive bleeding, high fever, or intercurrent disorder in which the most rapid possible non-surgical emptying of the uterus is desirable. He believes that by means of this drug, operative interference might many times be avoided or, when required, facilitated. He proceeds as follows: 1 gm. of quinine hydrochloride is boiled with 20 c.c. of distilled water until sterile. Of this solution 10 c.c., containing 0.5 gm., are injected intravenously; and the other 10 c.c. intramuscularly (combined injec-

(6) Jour. Lab. and Clin. Med., April, 1921.

(7) Therap. Halbmonatsch., Jan. 1, 1921.

tion). The injections should be administered as slowly a possible as they are frequently followed by nausea, vomiting, tinnitus aurium and deafness, symptoms which are less marked when the injection is given slowly. In any case all of these symptoms disappear after a while.

Quinine is incapable of initiating contractions in the quiescent gravid uterus; but, when pains once initiated have diminished or ceased, then quinine frequently brings about surprising improvement in uterine contractions, so as to cause expulsion of the fetus and placenta, or at least the fetus. On the other hand, in case of incomplete abortion, the combined quinine injection never succeeded in causing expulsion of placenta or other residue. The author considers this use of quinine of special value to the general practitioner.

DIURETICS

Water Diuresis. E. K. Marshall⁸ investigated the influence of the greatly increased ingestion of water upon the elimination of urea, creatinine and chlorides. His results are in contradiction to most of our present-day theories. His conclusion of practical importance is that while we may increase the urine volume to an enormous extent, even twenty-fold or more, the solids investigated are by no means proportionately increased; thus, the creatinine elimination is not increased to a measurable degree. The elimination of urea is increased definitely but never more than two-fold, while the chlorides are variable in their elimination and generally less marked in increase than urea.

“The increases in urea and chloride do not correspond with the maximum increase in water excretion, in fact at the height of the diuresis the chloride elimination generally decreases. During water diuresis the chloride of the plasma may decrease, while the concentrations of urea and creatinine in the plasma do not vary appreciably.”

Sugar Diuresis. As the result of experiments, Brunn⁹

(8) Jour. Pharm. and Exper. Therap., October, 1920.

(9) Centralbl. f. inn. Med., Sept. 18, 1920.

finds that the ingestion of sodium chloride with water causes less fluid to be secreted than when water is given alone. Additions of 12, 18, and 24 gm. of sodium bicarbonate checks diuresis in much the same manner as sodium chloride. The addition of sugar to water causes an increase of diuresis; thus, 100 gm. of sugar to 1 liter of water produced 1,600 c.c. of urine in four hours.

Potassium Chloride as Diuretic. L. Blum, E. Aurel and R. Lévy¹ found that, while sodium chloride causes retention of fluids, potassium chloride acts as a powerful diuretic, even in cases in which other diuretics had failed, excepting in a case of amyloid kidney. The initial dose is 1 gm. This may be increased to 5 and 7.5 gm. in the twenty-four hours unless symptoms of intolerance manifest themselves. These are diarrhea, weakness, fatigue, headache and chilliness. If the circulatory system is diseased, there may be dyspnea, cyanosis, extrasystoles, a sensation of constriction and morbid apprehension, and fall in blood-pressure.

Diminution of Urine Secretion from Excessive Dosage of Diuretics. G. Stroomann² cites a number of nephritic cases in which a sudden diminution in the quantity of urine occurred after an initial diuresis, as the result of continued ingestion of xanthine bodies, especially theocin. The return of diuresis could then only be brought about by stopping the administration of the theocin or by lessening its dose, or by the use of the weaker diuretin. The author refers to the animal experiments of Loewi, Barcroft and Straub, in which repeated injections caused cessation of diuresis even though the diuretic effect of sodium chloride was still obtainable. We have to deal here with a specific failure of action of the xanthine bodies. Owing to our inability to assign the action to a more specific cause, we might speak of it as fatigue. Stroomann has come to prefer diuretin to theocin especially in cases of sclerotic kidney lesions. He employs this remedy in a course of closely succeeding dosage, beginning first in the afternoon at perhaps 2 p. m. and giving, at intervals of one to one-and-one-half hours, doses of 0.5 gm. up to eight times,

(1) Bull. d. soc. med. d. hôp., June 24, 1921.

(2) Therap. Halbmonatsh., July 1, 1921.

rarely more. Theocin is given in a similar way in doses of 0.1 gm. twice up to 0.2 gm. three or four times to avoid fatigue. It is best to repeat these doses only after intervals of two or three or more days.

Digitalis has likewise produced diminution of the secretion of urine when used in excessive dosage or when used in combination with one of the above mentioned xanthine bodies in dosage in which the latter gave satisfactory diuresis. The author is inclined to ascribe this action to vasoconstriction by digitalis, occurring because of excessive irritability of the blood-vessels.

[In these days of a tendency toward high digitalis dosage, caution in the presence of nephritis may well be emphasized.—Ed.]

Theobromine in Epilepsy. Carl Pototzky³, having found that theobromine preparations such as diuretin increase the secretion of salts in the urine even in animals with sodium chloride deficiency, suggests the use of theobromine in epilepsy alongside of salt poor diet and bromides, in order to hasten the appearance of bromide action. The use of this method would be particularly indicated in status epilepticus.

RESPIRATORY STIMULANT

Lobeline as a Respiratory Stimulant. E. Rominger⁴ reports observations on about ninety cases of serious respiratory disturbance in children in whom he was able to demonstrate a stimulant action on the respiratory center from pure crystalized lobeline (Ingleheim). This action occurred even when the respiratory center was depressed from carbon dioxide, as in the second stage of asphyxia. Definite results were obtained with this remedy in severe disturbances of respiration in the course of pneumonia, in collapse from various causes, and in depression of the respiratory center due to the use of narcotics such as chloral hydrate in the treatment of convulsions.

He reports a case of paralytic apnea with extreme cyanosis occurring at the beginning of a trache-

(3) *Therap. Halbmonatsh.*, April 1, 1921.

(4) *Ibid.*, June 15, 1921.

otomy in an intubated child suffering from diphtheritic laryngeal stenosis. Rapid introduction of the tracheal tube, artificial respiration, and injections of camphor were all negative in their effect. About two minutes after a subcutaneous injection of 3 mg. of lobeline, regular deep respiration set in, much to the surprise of the attending physicians, who had considered the case hopeless; and in a few minutes the child was on the road to recovery. After subcutaneous injections of from 1 to 3 mg. of this alkaloid, Rominger states that he has never seen any untoward results or tendency to cumulative action. He believes that this remedy might also be of particular value to surgeons in the accidents of anesthesia and to obstetricians in the treatment of asphyxia of the new-born.

CARDIANTS

DIGITALIS AND ATROPINE

Cardiac Pharmaco-therapy. In a review article R. Offenbacher⁵ discusses the present status of the use of circulatory stimulants in Germany. According to an old rule, digitalis is contraindicated in high blood-pressure, bradycardia, and impairment of conduction in the bundle of His as well as in perpetual arrhythmia and pulsus alternans. In point of fact, however, digitalis has been favorably used in nearly all of these conditions, though it is well to use it cautiously in such cases. In cases of high blood-pressure not only did digitalis produce no further rise in pressure, but frequently a lowering of the tension; and with it improvement in the circulation. In cases of transmission disturbance in the bundle of His, digitalis has been successfully used; though a combination of digitalis and atropine might be more advisable—the atropine being used to lessen the irritability of the vagus. In perpetual arrhythmia, digitalis is sometimes successful and sometimes fails. In the latter class of cases the use of quinidine might be helpful. Though digitalis produces pulsus alternans when given in overdose, cases have been found in which

(5) *Therap. Halbmonatsh.*, Nov. 1, 1920.

patients with *pulsus alternans* were generally improved by the cautious administration of *digitalis*. The drug is given in doses of from 0.3 to 0.4 gm. a day in form of powder, the dose to be reduced to 0.05 gm. as soon as compensation has been established. For intravenous use, the author has found *digipuratum* or *digifolin* satisfactory; and prefers these to *strophanthin* which he considers dangerous.

Squill has not been satisfactory except in a few cases of mild thyreo-toxic cardiac weakness.

In obstinate cardiac dropsy, *theacylon* tablets or *theophyllin* may be useful. In some cases intravenous injection of 0.30 gm., has been quite satisfactory. Special attention is called to the value of large doses of urea in cardiac dropsy. In some cases, after *digitalis*, *theobromine* preparations and *potassium acetate* had failed, the administration four times daily of from 15 to 25 gm. of urea in twice the amount of water caused the onset of copious diuresis without increase in the blood nitrogen even in cases of nephritic dropsy.

In common with other continental authors, *Offenbacher* thinks very favorably of the hypodermic use of camphorated oil especially when mixed with an equal amount of ether, 2 c.c. being injected many times a day. He has of late been induced to try the use of *strychnine nitrate* in doses of 1 to 2 mg. because of the popularity of this remedy in the English-speaking countries, and believes that he has seen good results from its use in influenza and pneumonia.

Subcutaneous injections of *epinephrine* the author uses only when other remedies fail and then with the greatest care, as he has repeatedly seen dangerous collapse with small pulse and great pallor and feeling of anxiety following its injection. This substance is also liable to produce extra-systolic arrhythmia in disabled hearts.

Action of *Digitalis* and *Atropine*. By a graphic study of the action of *digitalis* and *atropine* on the peripheral circulation in man, *I. Harris*⁶ arrives at conclusions somewhat at variance with opinions generally held regarding the action of these drugs. His findings are

(6) *Lancet*, May 21, 1921.

especially valuable as they were obtained on human beings with diseased hearts, who evidently give different reactions from those obtained in a dog with a healthy heart.

“Under the influence of digitalis, the diastolic pressure becomes lower and incidentally the systolic, while pulse pressure rises. The decline of the diastolic pressure is not due to a diminished output of the heart—the contrary is the case. Neither is the low diastolic pressure due to dilatation of the arteries. The conclusion is that the blood-stream leaves the arterial circulation at a greater rate than under normal conditions. The corollary to this conclusion is that under digitalis the heart contains at the beginning of the systole a greater amount of blood than before. The quickening of the pulse observed in the latter stages of digitalis action is due to the fact that, in a shorter time than normal, the intracardiac pressure is sufficiently high to excite contraction.” The angina-like pain from which patients suffer who are under the influence of an overdose of this drug and the fatal issue which sometimes, though rarely, attends its use, is to be attributed to high intracardiac pressure.

The dose of digitalis required to bring about an acceleration of the pulse rate stands in a definite relation to the condition of the myocardium. If the latter is degenerated, a small dose of digitalis is sufficient to bring about a quickening of the pulse rate.

Action of Atropine: Within half an hour after the hypodermic injection of $\frac{1}{100}$ — $\frac{1}{75}$ of a grain of atropine, in the majority of cases under observation, the systolic pressure fell and the pulse pressure became diminished; the diastolic pressure, too, fell, but to a lesser degree than the systolic, and the pulse rate became lower. In all essentials, the effect of atropine is the same whether the patient has been under the influence of digitalis or not. If the pulse frequency has increased owing to the action of digitalis, the administration of atropine will considerably lower the pulse rate. Similarly, under atropine any cardiographic evidence of digitalis poisoning which may be present will disappear. Atropine in doses of $\frac{1}{50}$ grain increases the pulse frequency, the

systolic pressure becomes lower and the pulse pressure diminished.

The slowing of the pulse rate brought about by atropine is evidently due to vagus stimulation. Apparently $\frac{1}{100}$ — $\frac{1}{75}$ gr. of atropine is not strong enough a dose to effect paralysis of the vagus endings. Vagus stimulation lowers the output of the heart; hence smallness of the pulse pressure results. The intracardiac pressure will be diminished under these conditions, owing to the feebler contraction. The latter circumstance would explain why the cardiographic signs which are attributable to a high intracardiac pressure disappear under this drug, and why in cases, which, under the influence of digitalis have exhibited an accelerated pulse frequency, an injection of atropine effects a lowering of pulse rate.

Atropine in dose of $\frac{1}{60}$ grain evidently paralyzes the vagus ending, the pulse rate is increased, the duration of the diastole being shorter than normal, the heart would not completely fill itself as is normally the case; the output per single beat would accordingly decrease, and one would get a relatively small pulse pressure under the circumstances. Evidently the total output of the heart under atropine is less than normal, otherwise we would be unable to explain the fall in the systolic pressure.

Slowing of the Pulse by Small Doses of Atropine.

H. McGuigan⁷ calls attention to the long-established but not sufficiently generally appreciated fact that small doses—the pharmacopeial average dose of 0.5 mg.,—slow the pulse; that larger doses 1 mg., still cause slowing with a tendency to irregularity; while with still larger doses, 2 mg., the slowing may be so transient as to escape notice. The slowing is due to stimulation of the vagus center and is observed clinically, most especially in exophthalmic goiter and in cases of vagotonia. It takes larger doses, 1 to 2 mg., to paralyze the vagus endings of the heart and presumably also elsewhere.

Digitalis Therapy in Cardiac Disease. Emil J. Pellini⁸ furnishes a report based on an analysis of 250 clinic cases, the period of observation ranging from three to

(7) Jour. Amer. Med. Ass'n., May 14, 1921.

(8) Ibid., March 19, 1921.

twelve months. He divides the series into non-digitalized cases, the digitalized cases with improvement, and the digitalized cases which are not improved.

His method of treatment is not at variance with the recognized standards of digitalis medication, but some of the more drastic measures are not applicable to the ambulatory cardiac patient, or if used must be modified. With each new patient requiring digitalis and not recently taking it, the first attempt should be thoroughly to digitalize him. Pellini starts with 30 drops, 3 drops to the minim, three times a day, and varies this dose later as the requirements arise. When full digitalization occurs he begins to decrease the dosage until the patient begins again to show the early signs of decompensation, when the dose is again increased. After several attempts with this procedure, he is finally able to obtain a minimum dose which would keep the patient digitalized, or, as it may be called, in "digitalis equilibrium." This dosage, when accurately determined, does not produce over-digitalization; and the patient can be kept under medication indefinitely. To maintain a digitalis equilibrium, 71 per cent. of the patients received between 20 and 30 minims a day. These figures compare favorably with those of Pardee of 22 minims a day. Patients not benefited by digitalis in doses of 45 minims a day should be in the hospital. One not infrequently meets a physician who believes that the giving of digitalis in more than very small doses to the ambulatory cardiac patient is attended with the danger of sudden death. The author does not agree with this. In none of the patients studied by Pellini, could death be attributed to digitalis. Hospital experience shows that many patients are forced to enter the hospital in a dangerous condition because of insufficient digitalis medication.

Action of Digitalis. How completely the results of pharmacologic research can be applied to patients is the question discussed by Drew Luten.⁹ A two-fold action is recognized on the basis of animal experimentation, (*a*) a stimulation of the vagus center in the medulla which tends to slow the rate, weaken systole, and pro-

(9) Jour. Amer. Med. Ass'n., Jan. 1, 1921.

long diastole; (b) a direct action on the heart muscle, increasing its tone, and thus causing relaxation to be imperfect while contraction is strengthened.

It has long been recognized that digitalis does produce vagus stimulation in the human subject. The important fact is that this stimulation produces effects by its depression of auriculoventricular conduction that are far more striking than any effect at the pacemaker. It is in this depression of conduction between auricle and ventricle that digitalis affords its most dependable and remarkable effect to benefit patients. Whatever may be said of other effects, there is unanimity of opinion here. The clinical condition in which advantage is taken of this depression of conduction by digitalis with such striking results is cardiac decompensation with auricular fibrillation, and auricular flutter. In this condition, with auricular fibrils contracting independently and sending down myriads of impulses to a distressed and overworked ventricle, the latter can not find sufficient rest. By depressing conduction, digitalis blocks off a number of these crowded and irregular impulses and thus allows the ventricle time to rest. There is no more pronounced and striking result in medicine than the rapid improvement in comfort of a patient with decompensation attending auricular fibrillation, with rapid heart rate, after a large dose or two of digitalis. Digitalis, here let it be remembered, gives its beneficent result, not because of any stimulating effect on the heart, but rather because it is a heart sedative. It helps the heart to rest.

Of the ability of digitalis to slow the heart rate of man through any stimulation of the vagus at the pacemaker, when administered in therapeutic doses, little more can be said, than that there is no such general agreement as there is in regard to its action in auricular fibrillation (and flutter) in depressing auriculoventricular conduction.

The effect on the heart muscle is still the subject of much speculation and investigation. That it has some effect on the heart muscle, there appears to be little doubt. At least the changes in the T-wave of the electrocardiogram, which occur under digitalis administration and disappear after its discontinuance, are now gen-

erally ascribed to an action of the drug on the heart muscle; but the exact nature of its action and the results of it are not clear. The important question, clinically, is: Does such action, if it occurs, result in increased cardiac efficiency? And to this question there is no very satisfactory answer. The question of the effect of digitalis on the output of the human heart must remain for the present an open one. The same thing must be said in regard to the question of benefit from digitalis therapy in cases of decompensation exhibiting a normal cardiac mechanism.

There is likewise some difference of opinion as to the effect of digitalis on blood-pressure. The prevailing view is that the drug in therapeutic doses has no appreciable effect primarily on blood-pressure and that any effects that occur are secondary, resulting from its cardiac action. High pressure, then, appears to be no contraindication to its administration.

Digitalis in High Blood-Pressure Stasis. A. R. Elliott¹ differentiates between those cases of high blood-pressure stasis in which there is kidney involvement, and those without kidney inadequacy. In the high pressure stasis of nephritis, digitalis has proved ineffectual. In the form without kidney involvement, digitalis may help the heart to rally; and it should be employed, although rarely will there be secured in the same degree the satisfactory results apparent in other forms of failing heart. If the heart muscle is found to respond to digitalis, its continued employment in optimum dosage appears necessary to maintain myocardial tonus. Such a heart, working ever on the verge of breakdown, can not be trusted to take care of itself without support. Rest and venesection are the only other measures found useful in these cases.

Variation in the Strength of Tincture of Digitalis. A. L. Smith² tested, by biologic methods twenty-five tinctures taken at random from the stocks of nineteen drug stores which may be considered as representative of tinctures dispensed in Lincoln, Neb. The tinctures

(1) Jour. Amer. Med. Ass'n., May 28, 1921.

(2) Neb. State Med. Jour., April, 1921.

of digitalis dispensed showed a marked variation in its strength. The samples varied from 19 to 99 per cent. of normal. The frequent impotency of the drug may be the cause of poor results in the administration of digitalis in cardiac disease. The best remedy at present evidently lies in dispensing only dated, standardized tincture of digitalis in the original one-ounce bottle. When a tincture of this type is used, the physician has an accurately potent drug to start with and he can either give it in large doses for a short period or gradually increase it until a definite cardiac response appears.

Tincture of Digitalis and the Infusion. S. Weiss and R. A. Hatcher³ find that, while the marc left after preparation of tincture of digitalis is inert, this is not the case with the marc left after preparation of the infusion. The official infusion therefore does not represent the drug completely. Hence the standardization of the leaf does not insure uniformity in activity of the infusion, and the variability of the infusion is at the expense of the more absorbable of the active principles. There is no essential difference in the amounts of the saponin bodies present in the tincture and in the infusion prepared from equal weights of the leaf, and therapeutic doses of digitalis do not contain enough to induce any undesired effects. The infusion prepared according to a simple method described in the article represents the activities of the leaf completely; hence it permits of uniformity when a standardized powder is used for making it. It may be used in place of the tincture in doses just ten times the volume of those of the latter. Such infusion, kept in completely filled and hermetically sealed bottles for more than two years and five months, retained its activity unimpaired.

Digitalis Dosage in Children. H. McCulloch and W. A. Rupe⁴ investigated the question whether the Eggleston dosage, based on body-weight, holds in children. Thirty-six children, healthy, so far as heart was concerned, but confined to bed or allowed limited periods in a wheel chair or sitting up, were given the tinc-

(3) Jour. Amer. Med. Ass'n., Feb. 19, 1921.

(4) Amer. Jour. Med. Sci., August, 1921.

ture in small amounts of water, at times with a little saccharin, four times a day on an "empty" stomach, by mouth; the total estimated dose was divided over a period of six days.

The authors conclude that Eggleston's formula, while it may apply to patients with heart disease, does not apply to children with normal hearts. Normal children require a larger amount per unit of body-weight to produce digitalization than do adults with heart disease. Up to approximately four years of age children respond more readily to digitalis than do children above this weight and age. The earliest sign of beginning digitalization was vomiting, which was often present before alterations in the electrocardiogram. The next most common changes were sinus arrhythmia and alteration in size and direction of the T-wave.

Dosage of Digitalin. Henry Beates, jr.⁵ deplors the lack of attention given to the fact that the name "Digitalin" is applied to several of its contained glucosides each of which constitutes a totally different substance with wide difference in dosage. The active principle of choice is digitalinum Germanicum of Merck, which in 0.015 gm. doses is equivalent to 1 c.c. of a standardized tincture and should be administered three or four times daily. This active principle practically represents the total equivalent or therapeutic activity of the crude drug, and differs from the latter in being almost entirely free from those associated properties which in full doses provoke gastro-intestinal distress. It possesses the great and superior advantage of uniformity of physiologic power, which galenical digitalis does not. In emergency, its hypodermic administration in from 0.03 to 0.06 gm. doses in from 10 to 20 c.c. normal salt solution will establish reaction in from twenty minutes to half an hour. It will cause cellulitis and even abscess, if it be not well diluted when given hypodermically. Its use intravenously has not been attempted, and because of the promptness with which it acts when given subcutaneously, the involved risks render it advisable to employ it in that way.

(5) Therap. Gaz., August, 1921.

PHYSOSTIGMINE

Physostigmine in Tachycardia. C. Lian and H. Welti⁶ report marked relief from palpitation in the tachycardia, of hypertonia of the sympathetic nervous system, as that occurring in exophthalmic goiter, from 1 mg. of eserine sulphate before one, two or three meals daily.

QUINIDINE

Quinidine in Auricular Fibrillation. Though digitalis is a most useful drug in the treatment of auricular fibrillation, it makes the pulse slower and more regular by lessening the conductivity of the bundle of His. It does not alter fibrillation of the auricles. Quinidine, on the other hand, is capable of restoring normal rhythm to the auricles in a considerable proportion of cases. Frey, in 1918, found this dextrorotatory stereo-isomer of quinine the most effective therapeutic agent in patients with auricular fibrillation. Because of its better solubility, quinidine sulphate, rather than the pure alkaloid, is used.

Hofmann (1920) has shown, in dogs' hearts perfused with solutions of the drug, diminution in the excitability of the auricular muscle to electrical stimulation. Strong induction shocks, effective in producing fibrillation of the auricles when the heart was perfused with Locke's solution, failed to elicit this arrhythmia when quinidine was added to the perfusate. The heart rate was slightly slowed.

W. Frey⁷ contrasts quinidine, which is capable of bringing the auricles to perfect rhythmic contractions in about 50 per cent. of the cases, with digitalis, which, though it slows the rate of ventricular contractions and makes the pulse more regular, never removes fibrillation of the auricle. Quinidine causes lessening of irritability and diminishes the power of contraction of the auricular muscle. The diminution of irritability is much desired; a marked lessening of muscular power, however, must be avoided.

Experience shows that quinidine must not be used in

(6) Bull. de la soc. méd., d. hôp., April 29, 1921.

(7) Therap. Halbmonatsh., Sept. 1, 1921.

profound cardiac insufficiency. Here, we must improve cardiac power by digitalis and other means until the threatening character of the condition has subsided. Then only is it wise to start the quinidine therapy. In cases of high blood-pressure and in chronic nephritics in whom auricular fibrillation occurs, quinidine therapy is usually disappointing. The earlier the use of quinidine is resorted to, the better the chances for success. In nearly every case of total arrhythmia due to auricular fibrillation, the disturbance first appears in attacks as a result of physical and nerve over-strain. In these, quinidine therapy is particularly indicated.

It is best to commence with a small dose say, 0.2 gm. of quinidine three times daily. The dose may be increased next day to four times daily 0.2 gm.; on the third day to five times daily of 0.2 gm.; on the fourth day to three times daily of 0.4 gm., which latter may be considered a large dose. This quantity may be maintained for from three to six days provided no disagreeable manifestations show themselves. Should dizziness, attacks of faintness, headaches, vomiting, or tachycardia above 140 beats, manifest themselves the treatment is to be interrupted.

It is inadvisable to combine quinidine with digitalis. The action of one lessens the action of the other upon the heart and unites in disturbing digestion.

Frey considers intravenous injections of quinidine dangerous and hopes that subcutaneous and intramuscular injections might be found useful, owing to the gastrointestinal disturbances appearing during quinidine administration.

E. Jenny⁸ succeeded in restoring normal rhythm in seventeen out of eighteen cases of auricular fibrillation and tachysystolia, by the action of quinidine. These results are better than all previously published. He gives 0.5 gm. of quinidine two or three times a day, and pushes the drug up to 2 or 3 gm. a day, providing there is constant supervision, and the drug is discontinued at the slightest derangement of vision or of hearing.

K. Faber⁹ reports a case in a man 59 years old with high blood-pressure who had been suffering from auricu-

(8) Schweiz. med. Wochenschr., March 24, 1921.

(9) Ugeskrift f. Læger, May 5, 1921.

lar fibrillation for three months with a marked pulse deficit. Quinidine was given, 1.20 gm. the first day and this dose three times the next day. The following day the dose was 0.30 gm. and the day after that 0.45 gm. But it was not until the sixth day that the arrhythmia disappeared. In a woman of 57 with old chronic heart disease, ascites and fibrillation, no benefit was secured from this drug in doses up to 2 gm. a day.

A. N. Hewlett and J. P. Sweeney¹⁰ report restoration of a normal rhythm in five of eleven patients, though in one case this continued for only a short period of time; and present the results obtained by others in the accompanying table.

CASES OF AURICULAR FIBRILLATION TREATED WITH QUINIDINE

| Author | Number of Cases | Normal Rhythm Restored | Recovering a Normal Rhythm Per Cent | Maximum Dose per Day Advised Gm. | Grains |
|--------------------------|-----------------|------------------------|-------------------------------------|----------------------------------|--------|
| Frey | 50 | 21 | 42 | 1.2 | 18½ |
| Bergmann | 9 | 6 | 67 | 2.0 | 31 |
| Wybauw | 25 | 14 | 56 | 1.5 | 24 |
| Klewitz | 13 | 1 | 8 | 1.0 | 15½ |
| Weisser | 11 | 4 | 35 | ... | .. |
| Boden and Neukirch | 17 | 6 | 35 | 2.0 | 31 |
| Haass, H. | 44 | 27 | 61 | 0.8 | 12½ |
| Benjamin and Kapff | 27 | 18 | 67 | 2.0 | 31 |
| Jenny | 18 | 17 | 94 | 3.0 | 46½ |
| Levy | 4 | 2 | 50 | 1.2 | 18½ |

From the accompanying table, it will be seen that, on the whole, the value of results obtained paralleled the size of the doses employed. Jenny, who obtained a remarkable number of successes, did not hesitate to use very large doses, while Klewitz, with his poor results, used small doses. When one recalls that the paroxysmal type of auricular fibrillation is essentially a recurring condition which tends in time to become permanently fixed, it is not surprising that relapses occur after the normal rhythm has been re-established by the use of quinidine. Quinidine like quinine, appears to be a cardiac depressant. Any improvement in circulation is apparently due to the restoration of normal rhythm and is

therefore an indirect effect of the drug. The degree of improvement depends on the degree to which the symptoms and the decompensation were dependent on the irregularity itself. Experience with paroxysmal fibrillation indicates that in some cases at least such symptoms as palpitation, precordial distress, and dyspnea become worse during the period of irregularity. This is particularly true if the ventricular rate is very rapid during the paroxysms. In such cases, the restoration of a normal rhythm might be expected to remove many of the troublesome symptoms. In other cases, and especially those in which there is a moderately slow and not very irregular pulse, the conversion to a regular rhythm could hardly be expected to make much difference. Finally, when symptoms depend less on the irregularity than on the changes in the heart muscle or valves, they would not be much altered by a change in rhythm. The patient may even become worse with a lessened diuresis.

Some patients are unusually susceptible to quinidine. A small preliminary dose is recommended for the first day. Hewlett and Sweeney usually give 0.2 gm. three or four times, the first day. After this they gave 0.4 gm. four or five times a day. They did not exceed a total of 2 gm. in twenty-four hours. The return to normal rhythm has occurred most frequently on about the third day of full treatment. After the fifth day, a few cases have become regular, although occasionally this has happened as late as the tenth day. The first course of treatment, therefore, should last about a week. If this fails a second course may be given as occasionally patients have become regular during the second course of treatment, when the first had failed. If the normal rhythm is re-established, the quinidine has usually been withdrawn by gradually diminishing the dose. In Hewlett and Sweeney's cases it was withdrawn abruptly. When relapses were frequent they were avoided, in some instances, by giving the drug regularly for an indefinite period of time. Digitalis and quinidine medication appear to be antagonistic, and it is generally inadvisable to combine quinidine and digitalis, as the administration of digitalis probably lessens the patient's chances for recovering regular rhythm. But as marked decompensation lessens the chances for recovering a normal rhythm,

patients with marked decompensation should first be given the usual treatment for decompensation, including digitalis. After allowing time for some of the digitalis effect to disappear, quinidine treatment may be instituted.

Untoward results: Loss of appetite with perhaps slight nausea or even vomiting, palpitation, increased heart rate, and a small and soft pulse are not uncommon effects of the drug. These symptoms may have to be disregarded to obtain the desired result. However, more serious symptoms may occur with or without warning. Alarming collapse has been recorded several times. Several fatalities have been reported, though in none of these was the drug clearly responsible for the deaths. At most, quinidine was only a minor factor in contributing toward the fatal result.

Walter W. Hamburger¹ reports seven cases of chronic auricular fibrillation, one case of paroxysmal auricular fibrillation, and one of auricular paroxysmal tachycardia, in each of which 0.2 gm. of quinidine was administered the first day as a preliminary idiosyncrasy test. The second day 0.4 gm. was given at 8, 12, 4 and 8 o'clock, and continued daily thereafter, until either a normal cardiac mechanism resulted, until sufficient had been given in the refractory cases to make it clear that no such effect could be obtained, or until some signs of intoxication had been produced. Of the eight cases of auricular fibrillation, four responded with the development of a normal cardiac mechanism (sinus rhythm) and four advanced cases remained unaffected. The case of paroxysmal fibrillation under quinidine showed distinct periods of shortening of the duration of the paroxysms, and gave evidence of prevention of recurrences during its administration.

No serious mishaps occurred in the observation of the "successful" cases. Various of these patients complained at different times of nausea, vertigo, transitory weakness, headache and tinnitus aurium. Two believed they had less cardiac palpitation, were more comfortable, and experienced improved sleep and appetite with the establishment of a sinus rhythm. Two noticed no

(1) Jour. Amer. Med. Ass'n., Dec. 3, 1921.

change. Most of them developed an early tachycardia of from 20 to 25 beats over their previous pulse rate and, subsequently, a bradycardia of from 45 to 55 with the establishment of a regular pulse. Two developed auricular and ventricular extrasystoles. The total urinary output in three patients was increased. The author feels it should be strongly emphasized that, for the present, quinidine sulphate is primarily of use in studying the mechanism of fibrillation of the auricles. He believes it desirable to sound a warning against the use of quinidine as a general therapeutic procedure for the treatment of various types of disorderly heart rhythm. When it is used, it should be considered a problem of clinical investigation, with careful observations and controls and judicious use in the question of dosage, as quinidine, apparently, is not without danger.

B. S. Oppenheimer and Hubert Mann² report twenty-two cases of auricular fibrillation treated with quinidine in nine of which the fibrillation was changed to a normal rhythm, while in two others the auricles responded by a change to either pure or impure flutter.

L. Cheinisse³ concludes, as a result of a review on the subject, that quinidine will arrest arrhythmia in a certain proportion of cases; but, sooner or later, the drug ceases to act, and the fibrillation becomes permanent.

THEOPHYLLIN

Euphylline Intravenously in Heart Disease. This drug is a combination of ethylendiamine with theophyllin which, in contrast to the latter, is extremely soluble in water. It is obtainable in 2 c.c. ampules containing 0.48 gm. euphyllin (of which 78 per cent. is theophyllin).

H. Guggenheimer⁴ advises that the commercial solution be diluted with 8 c.c. of double distilled water, whereby local irritation is avoided and if the injection is made sufficiently slowly—in about 2 or 3 minutes—disagreeable side effects can be avoided. If the injection is made too rapidly great increase in pulse rate with

(2) Jour. Amer. Med. Ass'n., Dec. 3, 1921.

(3) Presse. méd., May 28, 1921.

(4) Therap. Halbmonatsh., Sept. 15, 1921.

sensation of heat and of palpitation is liable to occur. It is best to warn the patient that these symptoms are likely to appear, and to ask him to notify the operator the moment any disagreeable sensation, such as that of heat, is felt, when the administration of the drug may be stopped for a moment until the sensation of heat has diminished, and the treatment may be concluded without ill results. He does not advise the intramuscular injection of this preparation because of its painfulness. Inasmuch as 0.8 gm. of theophyllin is considered a maximum daily dose, not more than two injections daily are advised; however, while often one injection a day suffices, the author would not hesitate to employ three injections daily, and for months if necessary, in cases requiring such dosage.

Euphyllin has proved of special value, he says, in angina pectoris and myocarditis and in conduction disturbances, all of which produce cardiac insufficiency due to deficient blood-supply to the heart. This group of cardiac disturbances is characterized by a relative or absolute slowing of the pulse in spite of cardiac incompetency. This combination of symptoms should make one cautious in the use of digitalis as it may cause still further slowing of the heart and impairment of cardiac nutrition. This need not be feared with euphyllin, as it causes increased rapidity of the heart beat and most especially as it has a marked tendency to produce vasodilatation, which also affects the coronary blood-vessels, an effect that has been established by animal experimentation.

ANESTHETICS

The Choice of Anesthetics. From the report of a recent Berlin meeting of the German Surgical Society⁵ the following maxims are culled:

Lumbar anesthesia causes a higher mortality rate than general narcosis and should, therefore, be restricted to definite indications. Its principal field of application is in the aged, more especially in arteriosclerosis, in amputations and in dislocations of the hip, and in fact in

(5) Jour. Amer. Med. Ass'n., July 23, 1921.

operations on the lower extremities and on the abdominal organs below the umbilicus. Epidural sacral anesthesia is quite as dangerous as lumbar anesthesia.

Local anesthesia by means of procaine with the addition of epinephrine is entirely harmless, but even here the maximal dose of procaine, namely, from 0.4 to 0.5 gm. must not be exceeded. It should be reduced in dealing with weakened patients. The principal field of local anesthesia is minor surgery of the extremities. For opening up the skull, general anesthesia is to be recommended. Local anesthesia may be employed for operations on the neck, also for strumectomy. In exophthalmic goiter, general narcosis is more appropriate on account of the excitable condition of the patient. For operations on the thoracic wall, local anesthesia may be employed; but for thoracoplasty general narcosis is better. In major abdominal operations, Braun recommends that first a scopolamine-morphine solution be injected, after which the abdomen may be opened under local anesthesia, and then during the remainder of the operation general anesthesia may be resorted to from time to time, as necessary.

For blocking the sacral plexus in prostatectomy and cancer of the rectum, lumbar, sacral and parasacral anesthesia are rival claimants for favor.

In almost all circles, ether is coming to be regarded as the best general anesthetic. It is being used by the drop method with an open mask. Primary death from heart failure does not occur with this method of narcosis. Intermittent narcosis should be avoided.

The injection of a narcotic before the anesthesia means a saving of 35 per cent. in chloroform and 40 per cent. in ether narcosis.

To prevent lung complications after anesthesia, patients should be encouraged to breathe deeply. Post-operative lung affections and embolisms can not be prevented by local anesthesia.

Chloroform is contraindicated in affections of the liver and in disturbances of the portal circulation.

Diminution of the circulation by the Klapp method has proved efficacious and saves large quantities of whatever anesthetic is employed.

Ethyl chloride anesthesia has proved its value; but in large doses ethyl chloride constitutes a poison and is not adapted for narcosis.

The various methods should not be regarded as rival claimants but as supplements of each other.

LOCAL ANESTHESIA

Anesthesia in Nose and Throat Work. The Committee on Local Anesthetics¹ of the American Medical Association, as a result of 315 replies obtained in return on fourteen hundred questionnaires sent out, present the following:

**Summary of Results of Investigation of Fatal Cases
Following the Use of Local Anesthetics.**

Deaths from local anesthetics for last two years*.... 27

The committee has received answers to letters inquiring as to cause of foregoing deaths from 22. These are:

| | |
|--|----|
| Cocaine (3 mistakes of nurse)..... | 11 |
| Cocaine and procaine..... | 5 |
| Procaine only | 3 |
| Apothesine and cocaine..... | 1 |
| Apothesine only | 1 |
| Alypin and cocaine..... | 1 |
| | 22 |
| No response from members repeatedly written to.... | 5 |
| | 27 |

* Only three of these were recorded in medical journals.

It will be seen that deaths from the administration of local anesthetics are vastly in excess of the number reported in the medical journals. In most instances, convulsions are the first indication of toxic effects; consciousness is never regained and death ensues within a comparatively short time.

Local Anesthesia in Eye Work.² The Committee on Local Anesthetics of the Section on Ophthalmology, of the American Medical Association, reports that the preponderance of evidence is in favor of a 4 per cent. solu-

(1) Jour. Amer. Med. Ass'n., Oct. 22, 1921.
 (2) Ibid., Nov. 26, 1921.

tion of cocaine as the local anesthetic for routine work. The reasons assigned for the preference are given as based on many years of experience, very satisfactory results from its use, and failure of other local anesthetics in one or more essentials to compare in reliability with cocaine. The dessication and disturbance of nutrition of the cornea produced by it are negligible or entirely avoided if care is observed in keeping the eyelids closed after the instillation of the cocaine solution and up to the time that the operative work is done.

Phenacaine (holocaine) in from 1 to 2 per cent. solution is used either frequently or occasionally in producing surface anesthesia for the removal of foreign bodies from the cornea, for local anesthesia in connection with therapeusis, for use prior to determining the tension with a tonometer, and for producing local anesthesia when a dilating effect on the pupil is to be avoided.

A greater percentage of the men use procaine (novocaine) in from 1 to 2 per cent. solution by infiltration methods for operations on the muscles, lids and sac, and enucleation, when general anesthesia is not to be employed. The addition of epinephrine not only adds to the efficiency of the solution by reducing the amount of hemorrhage during the operation; but, through constriction of the blood-vessels, it lessens the absorption of the anesthetic agent and hence reduces the possibility of toxic effects.

Apothesin was condemned as unsatisfactory for ophthalmic work. Alypin was pronounced too feeble as well as too toxic, and the same objection was raised concerning beta-eucaine. Acoïn was considered by two as painful to use. Even phenacaine, which next to cocaine is most in favor, offers the objection that it produces irritation of the eyes, and must be prepared and kept in porcelain receptacles.

Five minutes after the instillation of either cocaine or phenacaine is considered sufficient allowance for superficial or surface anesthesia, whereas fifteen minutes, or following immediately after the fourth instillation of either cocaine or phenacaine at three-minute intervals, is sufficient allowance for the deep anesthesia required for cataract extractions and other operations upon the eye-

ball. The anesthesia lasts from fifteen to twenty minutes, or long enough for the average ophthalmic operation. In infiltration anesthesia, most operators allow from eight to ten minutes subsequent to the last injection to insure the maximum anesthesia, and they count upon holding the anesthesia for from thirty to thirty-five minutes.

All the observers agree that local instillation of cocaine in the eye allays irritation and reduces vascularity, whereas phenacaine produces the opposite effect. Most of the ophthalmologists offset the congesting effect of phenacaine by adding epinephrine to the solution. Owing to the fact that only small amounts of local anesthetics are used in ophthalmic practice, the occurrence of toxic effects is rare. The toxic symptoms observed and described are at first a sense of exhilaration, followed by giddiness, oppressed breathing, pallor, nausea, clammy perspiring skin and general weakness. All these symptoms usually disappear promptly after the patient lowers the head even with the knees, or is placed in a reclining position. No difference was observed in the anesthetic effect produced by the solutions that were sterilized by boiling and those not subjected to heat. Nothing but freshly prepared solutions of cocaine are used in operative work. Solutions will remain active for a much longer time, if 5 grains of boric acid are added to each ounce of the solution.

Synergists and Antagonists of Cocaine. A. L. Tatum³ investigated by animal experimentation the question of the point of action of cocaine and concludes that it increases the effects of epinephrine and of electric stimulation of the sympathetic nerves in the region investigated, namely the splanchnic and the cervical sympathetic; and that these increased effects are due to an increased responsivity of the peripheral neuromuscular mechanism. The practical lesson to be learned from these experiments is the synergism between cocaine and epinephrine, both of which act upon the same structures, to which must be added that stimulation of epinephrine production occurs as has incidentally been brought out by Tatum's experiments.

(3) Jour. Pharm. and Exper. Therap., September, 1920.

Karl Mayer⁴ has arrived at the conclusion that morphine is by no means antagonistic to cocaine, as stated in some text-books; that, contrarily, it increases the toxic action to a considerable degree. He found that frogs that received cocaine only had a much better chance of recovery than those that received morphine and cocaine. He also refers to experiments on guinea-pigs and rabbits by Agda Hofvendahl (1920), which led to a similar result.

He finds, on the other hand, that calcium regularly lessens the toxicity of cocaine in experiments upon frogs, as well as in observations upon the isolated heart. He contrasts this antagonistic effect of calcium with the synergistic action of potassium in relation to cocaine; and suggests that it might be due to the colloid condensing action of calcium as compared with the colloid dissolving action of potassium.

Caffeine Intrathecally in Syncope of Spinal Anesthesia. R. Bloch and Hertz⁵ found by experience with four cases, that the injection of about 0.20 gm. of caffeine injected directly into the spinal cavity, as was the anesthetic itself, resuscitated patients almost at once even after complete arrest of the respiration.

Local Anesthesia in Treatment of Sacro-Coccygeal Pain. Two different modes of attack by means of local anesthesia for the relief of pelvic backache are described in current literature. Nüremberger⁶ gives the following technique for the symptomatic treatment of pains regarding the etiology of which a careful examination gives no clue. He produces presacral anesthesia by the injection of 0.1 per cent. of beta eucaine solution as follows: With the patient in the lithotomy position with slightly raised pelvis he administers light ethyl chloride anesthesia to prevent even the slight pain of the procedure. At the level of the tip of the sacrum and from 1.5 to 2 cm. to the side, introduce a 15 cm. (6 inch) needle horizontally and parallel to the median line, until one strikes bone. The tip of the needle is now in the vicinity of the first sacral foramen. Having with-

(4) Schweiz. med. Wochenschr., Aug. 18, 1921.

(5) Presse méd., July 2, 1921.

(6) Münch. med. Wochenschr., 1921, p. 230.

drawn the needle slightly, inject with considerable pressure 20 c.c. of the solution. Then withdraw the needle for a few centimeters and raise up the barrel of the syringe by about 15 degrees so that the tip is lowered. If one now pushes the needle in the new location one arrives in the second sacral foramen. Here again 20 c.c. of the solution are injected. By further withdrawal and by advancing the needle more perpendicularly one is able to inject another 20 c.c. in the vicinity of the third sacral foramen, and by further repetitions of the manuever one finally injects in the vicinity of the fourth and fifth sacral nerves and the coccygeal plexus. If both sides have to be injected, it is best to employ only 70 c.c. on each side instead of 100 c.c. which might be employed for unilateral injection. Nüremberger believes that this method might be useful in climacteric pelvic pain, in posterior parametritis, coccydynia, and in sciatica. He reports the cure of seven cases.

In pelvic pain produced by shrinkage of the pelvic connective tissue at the menopause, Novak⁷ advocates the injection of 60 c.c. of 0.1 per cent. procaine-epinephrine solution into the parametric and paravaginal tissue to interrupt the nerve conduction and loosen shrunken connective tissue by means of the edema produced by the injection. He reports five successful cases.

The Stability of Benzyl Alcohol Solutions. D. I. Macht, and A. T. Shohl⁸ investigated the keeping qualities of aqueous solutions of benzyl alcohol varying from 1 to 4 per cent.; as next to efficiency and low toxicity, in connection with which the authors believe benzyl alcohol ranks very high, the keeping qualities are of decided importance in the practical use of local anesthetics. Benzyl alcohol permits sterilization by boiling. It is also a powerful antiseptic and keeps sterile indefinitely. However, the activity of its solutions has been found to deteriorate when they are kept in soft or alkaline glass, such as flint or amber colored bottles. On the other hand, solutions kept in non-soluble pyrex glass preserve their anesthetic properties. It is evident that this change

(7) *Centralbl. f. Gynäk.*, 1921, p. 417.

(8) *Jour. Pharm. and Exper. Therap.*, August, 1920.

occurs by reason of slow oxidation of benzyl alcohol to benzaldehyde and the rapid oxidation of the latter to benzoic acid which takes place in an alkaline and not in an acid medium. Hence, solutions of benzyl alcohol should be kept in hard glass bottles preferably with a buffer solution (acid sodium phosphate).

Phenolized Scalpel. E. J. Clemons⁹ makes incision of abscesses painless by dipping a dry sterile scalpel blade in pure phenol. The point of the back of the blade is then passed over the line of intended incision, so as to mark it with phenol, thus anesthetizing the skin. A few seconds later the instrument is again dipped in the phenol and the tissues are incized very slowly, the scalpel being moved up and down as in cutting with a saw. As the film is rubbed off by the tissues or is washed off by the blood, phenol has to be renewed by dipping the instrument in the phenol as often as it is necessary.

GENERAL ANESTHESIA

The Oxygen Percentages of Nitrous Oxide-Oxygen Anesthesia. Dorothy A. Wood and Mary E. Botsford¹ credit Dr. Horace Andrews of Chicago as the first to call attention, in 1868, to the fact that nitrous oxide and oxygen was a much more satisfactory mixture than nitrous oxide alone or in combination with air. In order to obtain the anesthetic state in average individuals, at least 80 per cent. of nitrous oxide in the inspired gas mixture is necessary. This leaves only 20 per cent. to be occupied by other gases; and, as the air contains 80 per cent. useless nitrogen and 20 per cent. of oxygen, it follows that in a mixture of nitrous oxide and air, the percentages are 80 per cent nitrous oxide, 16 per cent useless nitrogen and 4 per cent oxygen. Sometimes 80 per cent. nitrous oxide is insufficient for relaxation and then the available oxygen must be crowded down to 3 and even 2 per cent. This necessitates very short operative procedures, for at least 10-15-20 per cent. of oxygen is necessary to support life for any length of time. It is therefore a great step in advance to use

(9) Amer. Physician, May, 1921.

(1) Calif. State Med. Jour., September, 1921.

nitrous-oxide oxygen, for then the mixture becomes 80-90 per cent. nitrous oxide and 20-10 per cent. oxygen.

The question arises, what is the percentage of oxygen in the mixture of nitrous oxide and oxygen that is safe? Connell found that any mixture less than 92 per cent. nitrous oxide and 8 per cent. oxygen was extremely dangerous and was useful only for momentary procedures; but even for this the use was condemned. He found the mixture 92 per cent. nitrous oxide and 8 per cent. oxygen, satisfactory for induction only. The zone recommended for abdominal surgery had the mixture of 80 per cent. nitrous oxide and 11 per cent. oxygen. In this zone the color of the patient was fairly cyanotic. The zone for surface surgery was 86-84 per cent. of nitrous oxide and 14-16 per cent. oxygen; here the color was normal. This zone with the addition of a slight amount of ether, when necessary, in suitable cases, is recommended as the best for all work, including abdominal surgery. A mixture of 80 per cent. nitrous oxide and 20 per cent. oxygen gives a subconscious analgesic state suitable for obstetrics. Any altered capacity of the blood to transfer oxygen, either in decreased rate of blood flow, or diminished hemoglobin content, would upset these zones; and persons with reduced hemoglobin, septic conditions, excessive or rapidly increasing weight, and growing children demand a greater percentage of oxygen in nitrous-oxide-oxygen anesthesia. In war surgery, Marshall and Cannon observed that patients operated on following severe loss of blood, or during shock, required a much greater percentage of oxygen for operative safety, than did normal subjects. With this as a basis, Jones and McPeck determined by the reaction of the exsanguinated guinea-pig that a blood loss of 20 per cent. demanded from three to four times the amount of oxygen that normal pigs demanded. This, therefore, is a very definite indication for using increased oxygenation with nitrous oxide, in the presence of recent hemorrhage.

Investigation carried on at the Mineola Flying Field, concerning the oxygen need of men, candidates for the aviation service, showed that as the oxygen percentages were decreased almost the same symptoms were noted in these men as are noted by anesthetists when the

oxygen content becomes insufficient during anesthesia, that is, an increase in respiratory volume and rate, an increase in pulse rate, an elevation in blood-pressure and the appearance of cyanosis. There are headache and nausea; and the counterpart of this we have in nitrous-oxide-oxygen anesthesia, as the post-anesthetic headache and vomiting in patients who have been somewhat cyanosed during the larger part of the anesthetic. Some men compensated so easily and so well, that they stood, for brief intervals, as low as 6 per cent. oxygen, while other men failed to compensate at all, or so poorly that they could not endure even the slight oxygen deficiency of moderate altitudes. In some subjects the first response began at an oxygen percentage of 17.9 per cent.; while the majority showed the first response between 15.5 per cent. to 16.5 per cent. This, therefore, means that in the average individual, when the oxygen content of the inspired mixture becomes less than 15 per cent., he must necessarily put out some effort to keep metabolic processes at the proper level, and it would seem that low oxygen percentages under anesthesia would be very similar in their effects to low oxygen percentages at high altitudes.

We then have to consider: Is the patient in question, under anesthesia, able to stand the necessary increase in pulse rate, respiratory rate and blood-pressure elevation? Is this particular patient one of those who would react well in the aviator tests?

There were three very definite types of reaction to the tests made: The optimum type showed no response until the reduced oxygen reached about 15 per cent. The second type showed response at 17.9 per cent. A third type is seen in elderly people in whom there may be practically no response. In these, the compensatory mechanism seems to be entirely overwhelmed. The counterpart to this type is seen in people who are unable to have ether added to the nitrous-oxide-oxygen mixture, for relaxation, and who may become cyanosed in an effort to keep them relaxed sufficiently for operative work; and then, although there is cyanosis, there may be no change in pulse, respiration or blood-pressure. These patients may then show post-operative myocar-

ditis, due to the fact that an insufficient amount of oxygen was supplied the heart muscle during the operation.

As a matter of practice, anesthetists ordinarily use the color of the patient's cheek, forehead, and finger nails as the guide to the safety of anesthesia, but Lundsgaard found that a considerable degree of oxygen unsaturation in the blood may be present without showing as cyanosis. He also found that cyanosis could not be produced in patients whose hemoglobin was less than 35 per cent. Hence an accurate means of gas delivery with an oxygen percentage seldom less than 15 per cent. is much to be preferred to the more or less haphazard methods usually employed.

The Danger Signals in Ethyl Chloride, General Anesthesia. A. E. Guedel² considers ethyl chloride third in value to nitrous oxid-oxygen and ether. He places it above chloroform in valuation. It is applicable for short operations and for induction of ether anesthesia when nitrous oxide and oxygen are not available. However, he has little use for it, except in emergencies. His report is based on observations made with the personal use of ethyl chloride in general anesthesia in about 2,000 cases, in the majority of which, he used a gauze-covered mask of the Yankauer type. Ethyl chloride in overdose produces one of two sets of symptoms; the spasm type and the respiratory depression type.

Approximately nine out of every ten patients overdosed with ethyl chloride manifest the spasm type. The first indication of approaching spasm is a sardonic grin. About the same time we notice a beginning contraction of the masseter muscles, and a beginning crowing of inspiration. This crowing, due to partially obstructed inspiration, is the real warning that the dose must be reduced. If the overdose of the drug be continued, the spasm progresses rapidly until, in about one or one and a half minutes more, it will have become a complete respiratory obstruction. The spasm, once inaugurated, develops so rapidly that cyanosis does not appear in the usual case until the obstruction is almost total. When it appears it develops rapidly, and

(2) Jour. Amer. Med. Ass'n., Aug. 6, 1921.

half a minute later the patient is black. The rapidity of progress of the spasm is apparently in proportion to the vapor tension of the ethyl chloride. In the spasm type the pupil does not dilate until respiratory obstruction is almost total. During the spasm period, the systolic blood-pressure is elevated to varying degrees in different patients. The diastolic pressure may follow the systolic upward, it may remain stationary, or it may fall as the systolic rises. The pulse rate increases during the spasm, as a rule proportionately to the increase of systolic pressure. There is a deepening of the spasm once inaugurated, for a period of a few seconds after the removal of the inhaler. This is constant, and the anesthetist knowing it will be saved some worry. As for resuscitation in these cases of peripheral respiratory obstruction, the problem is the same as with overdose under any other anesthetic agent, namely, the removal, from the blood and tissue cells, of the excess of the drug. However, in the spasm type this is not an easy task because of the rigid contraction of the masseters. The mouth must be opened, the tongue pulled far out and vigorous chest compression made. Even with the mouth open and the tongue out, there is still a great deal of obstruction. However, the rapidity of elimination of ethyl chloride makes the resuscitation successful in the good cardiovascular type. The author has not seen a death under ethyl chloride but, in his early use of it, he has been more than once badly frightened. With knowledge of this action, there is ample warning from the beginning spasm to avoid the more serious aspects of it by the immediate removal of the drug, as soon as the spasm is noted. In many cases, it is difficult to maintain anesthesia without many times entering the beginning of this spasm. The beginner with this drug should always insert a substantial mouth gag before starting the anesthetic.

The depression type is a progressive central respiratory depression. From the onset, the respiratory effort grows less both in volume and in rate. The volume depression is greater than that of the rate. With the continuance of the drug in overdose, this depression progresses to a complete respiratory paralysis in from one

half minute to two minutes, depending on the patient and the vapor tension of the drug. The patient is perfectly relaxed, in every way. The picture during the deeper degrees of depression is one of collapse. The color is ashen; the pupils widely dilated; and the respiratory effort, if present, is quite discouraging. The picture resembles that of cardiac syncope; but the pulse belies the picture for, although slowed in rate, it is of good quality and regular. The blood-pressure does not fall to an extent that the change can be detected by palpation. As with the spasm type, this respiratory depression may repeat, during the same anesthetic, as often as the patient is overdosed. Following recovery from this depression, the anesthetic may be continued as usual. To the observant anesthetist there is ample warning of the approach of this depression; and there is no need that it be carried to the degree of total paralysis of the center. If total paralysis should occur, however, resuscitation is simple. There is no respiratory obstruction, and two or three forceful, manual compressions of the thorax serve to eliminate the excess of the drug from about the respiratory center, and automatic respiration is re-established, to carry itself to the anesthetic normal in from one to four minutes.

Treatment of Depression of Circulation in Anesthesia. E. I. McKesson³ insists that no one is able to diagnose varying degrees of the progress of circulatory depression by merely feeling and counting the pulse. The sphygmomanometer is the only instrument that we have for definitely indicating the pressure elements of the circulation; and to anesthetize for major operations without its use is inexcusable.

Clinically, we may divide depression into three stages or degrees by the pulse-blood-pressure reactions or relations: The first stage is characterized by either a small increase in pulse rate without a corresponding increase in systolic pressure or a small decrease in blood-pressure without a decrease in pulse rate. The second stage is usually characterized by an increase in pulse rate and a decrease in blood-pressures. This stage is regarded as dangerous and is the signal for the anesthetist to have

restorative measures ready for immediate use should it merge into the third stage. In some instances, at least, treatment should be started at this time, and the surgeon should always be advised so that he may be prepared to modify his operation if it becomes necessary. The third stage, is a further development of the second, and in the adult is characterized by a progressively increasing pulse rate above 100 and decreasing blood-pressure below a systolic of 80 mm. and a pulse pressure of 20 mm. and less.

The onset of the third degree during an operation indicates the gross incompensation of the elements of circulation—the inability of the patient to withstand the depressing influence on the cardiovascular system and marks the moment when active measures are to be instituted to assist the exhausted circulatory muscle, if not already undertaken. This is the condition of the circulatory system when the classical signs of shock become manifested. It appears from clinical observation that few patients recover if the third degree be allowed to continue progressively over a period of more than from twenty to thirty minutes. Twenty minutes is a short time in which to act, when it is remembered that in the average hospital more than half an hour passes before normal saline solution can be or rather is actually running into the vein of the patient after it has been ordered. Its late introduction is quite as ineffective in restoring the patient as an insufficient quantity. Of the measures employed to restore blood-pressure-pulse ratios compatible with recovery from a third degree depression, normal saline, Ringer's or Fisher's solution have given best results. To this should be added warmth to the extremities. Digitalis derivatives and camphorated oil may be employed with doubtful benefit. Saline solutions have failed in shock; first, because administered too late; second, because the proper quantities have not been administered, and third, because they have been used subcutaneously. The patient may show decided improvement after 500 c.c. have been administered, but it is necessary to bring the systolic pressure up to within from 10 to 15 mm. of the patient's normal pressure and to maintain this pressure by slow additions of the saline

solution until the operation has been completed. After the patient has been put to bed, the blood-pressure should be watched, and intravenous injections repeated if the rectal drip fails to maintain the pressures during the next twenty-four to thirty-six hours, or longer. The quantity of physiologic sodium-chloride solution which should be administered intravenously must be determined by the sphygmomanometer, and not measured by volume except as a matter of record. It varies from 300 c.c. to 2,500 c.c. at one time. Physiologic sodium chloride solution does not always elevate the diastolic pressure in its normal proportion to systolic pressure, *i. e.*, while the vascular system is filled, the arterial tonus does not recover so rapidly as the cardiac muscle. For this reason one should also watch the relation of the pulse pressure to diastolic pressure—its normal ratio is as 1 is to 2—and should stop the saline if the pulse pressure begins to exceed the diastolic pressure just before the desired systolic pressure is attained. In this respect, Fisher's solution is better for intravenous injection in shock.

Epinephrine Danger in Chloroform Anesthesia. W. J. R. Heinekamp⁴ shows by experiments upon dogs that chloroform, whether inhaled or injected intravenously, produces a toxic effect upon heart muscle resulting in dilatation and weakness. If epinephrine be injected at this point, the heightened blood-pressure induces paralytic dilatation and occasionally fibrillation of the heart. In one experiment, atropine produced identical results. The cause of this phenomenon is evidently the great increase in peripheral pressure that produces an extra high aortic pressure against which the weak heart can not empty itself. Resuscitation can not be effected when once the heart is in fibrillation. However, if fibrillation has not occurred, cardiac massage may restore automatic beating. The important fact to remember is that epinephrine is contraindicated whenever chloroform is employed, and chloroform whenever epinephrine is used.

Danger of Magnesium-Sulphate Solution as an Aid in Anesthesia. A fatality in a well-nourished woman, aged 35, who received a hypodermoclysis of 310 c.c. of

(4) Jour. Pharm. and Exper. Therap., November, 1920.

a 4 per cent. c.p. magnesium-sulphate solution, and two hypodermics of 8 mg. of morphine, preceding nitrous-oxide-oxygen anesthesia for removal of a fibromyoma of the uterus, is reported by A. H. Curtis.⁴ The patient rested comfortably for six hours. Thereafter she was distressed by persistent nausea and repeated vomiting of small amounts. There was a gradual increase in the pulse rate and moderate elevation of the temperature. Gastric lavage failed to relieve the symptoms. Urine was satisfactorily voided for eighteen hours; then it became very scanty, was deeply stained with bile, and contained many hyaline and granular casts. After forty-eight hours there was pronounced jaundice; the pulse was 158; the temperature, 102.8 F.; leukocytes, 16,000; breathing labored, but not notably accelerated. Death occurred twelve hours later, after a period of marked prostration.

A postmortem examination by Dr. Edwin Hirsch, demonstrated marked jaundice, marked acute fatty changes of the liver, marked cloudy swelling of the parenchymatous organs, multiple petechial hemorrhages of the pleura, pericardium and endocardium. There was no peritoneal infection. Cultures of the heart's blood and pericardial fluid were sterile after incubation. The magnesium content of the liver after deducting the amount normally present in human liver represented 5.33 gm. of $MgSO_4 \cdot 7H_2O$.

That magnesium sulphate injections are not without effect in the body tissues is known from observation on lower animals, as such injections produce hyperglycemia and glycosuria due to changes in the liver.

Study of the fatal case reported indicates that magnesium-sulphate solution sometimes produces profound changes in the liver and can not be considered a safe anesthetic for general use.

Scopolamine-Morphine Anesthesia in Surgery. During a period of fourteen months approximately 1,000 patients were operated upon by M. Thorek⁵ under scopolamine-morphine anesthesia, supplemented either by ether or nitrous oxide, without a single death having

(4) Jour. Amer. Med. Ass'n., Nov. 5, 1921.

(5) Illinois Med. Jour., June, 1921.

been caused by the method of anesthesia practiced, which was as follows:

“Thorough examination of the patient with special reference to the cardiovascular and renal apparatus. Preparation of the patient the day before the operation. Have the room darkened and absolute quiet enforced. In wards, screens should isolate the patient from the rest of the ward. The external auditory canal of the patient is plugged with cotton and all noises and disturbances excluded. The drugs used are scopolamine hydrobromide 0.0006 gm. and morphine sulphate 0.01 gm. This dose is repeated once: the first dose is given three hours and the second dose one hour before the operation. The above dosage is used in patients between the ages of 15 and 60 years. The dose is decreased according to the age of the patient. In those of 70 and over, 0.0003 gm. scopolamine and 0.004 gm. morphine are used—not more than two doses. Those patients who have not reached the age of 15 are not given scopolamine. This form of anesthesia is supplemented by nitrous oxide-oxygen or ether, or a mixture of both, depending on the type of the case and indications or contraindications in the respective patients. Chloroform has been banished. The method is not used in obstetrical surgery.”

Thorek considers scopolamine-morphine anesthesia, supplemented by nitrous oxide or ether, a distinct advance in narcosis; and, with experienced supervision, perfectly safe. The advantages of this method of anesthesia are: suppression of operative fear in the patient; absolute loss of consciousness; amnesia as to preparation, etc., incident to the operative procedure; continuation of sleep for from four to eight hours after the operation is completed; elimination of postoperative nausea, vomiting and the harmful straining incident to it; complete relaxation of the viscera and prevention of such unpleasant complications as pneumonia and shock.

To obviate the postoperative acidosis and relieve the dryness of the mouth and thirst, as well as to replenish the vascular system with fluid, the patient is given, directly he is put to bed, an enteroclysis of 3 liters of tap water at about 100° F. to which 16 gm. of sodium

bicarbonate have been added; in shock, with the addition of some brandy [alcohol would do as well.—Ed.] It goes without saying that when operations are done about the vagina, rectum and perineum, as well as in cases of perforative appendicitis and extensive resection of the lower bowel, the enteroclysis is omitted. To avoid excessive distention, the colon tube should never be introduced higher than three inches in the lower bowel. This is imperative.

HYPNOTICS

Uses and Doses of Hypnotics. F. Wyatt-Smith⁶ believes that we have far too many hypnotics, just as we have a bewildering number of members of every other group of medicaments. Surely it is better to learn something definite about the powers and behavior of two or three dozen plain and simple drugs, which is all that most men really have time for in a medical life, than to trifle with some hundreds of the curiosities of medicine.

Opium should never be regarded as a hypnotic, for no hypnotic ever leads to such craving for itself as can not be removed by the simple process of substituting another for it until the cause of the compelling insomnia is withdrawn. Except in the last stages of hopeless orthopnea, opium ought not to be used, even as an analgesic unless the case is hopeless or the cause of the pain is known to be transitory or quickly removable.

The bromides must be denied the right to masquerade as hypnotics. We should reserve them only for epileptic and gynecologic practice.

Chloral is the cheapest hypnotic for prolonged use, and is probably not very dangerous even in fatty heart. The author has often used it in such cases in doses of at least 20 grains three times a day for many days in succession, without reason to suspect injurious result. He fears we have too many who prefer standing by with folded hands while restless patients exhaust themselves to death rather than take some risk in trying to save their lives.

Barbital (veronal), within the pharmacopeial dosage, has proved almost useless in his hands. Paraldehyde, which is almost non-toxic Wyatt-Smith gives in half ounce doses every four hours. It is a useful drug for quick action, though it has the drawback of an objectionable taste which makes it difficult to get down in bulk, especially in resistive individuals. As a chronic "night-cap" for patients for whom a dram or two is sufficient, it is generally the most satisfactory of all its congeners.

Sulphonal, in many ways the most useful of the hypnotics, holds a place only second to hyosine in the dread with which it is regarded by prescribers. Its greatest disadvantage is its insolubility, and hence its slow absorption and delayed action. Its second is its great cost. It has one great advantage over the other hypnotics in its tastelessness, and hence its easy administration in bread and butter without the patient's knowledge. It appears to be quite safe in doses up to at least a dram a day. The best way to administer it is in three evenly divided doses through the day, reducing these till they procure sleep only at night and not drowsiness in the day as well, unless we wish to obtain its very soothing effect on the general mentality of the patient. Given in this way it is a decidedly useful mental sedative. In a case of acute mania, we may begin with a mixture, given by tube if necessary, of perhaps 2 ozs. of castor oil, 2 minims of croton oil, $\frac{1}{2}$ oz. of paraldehyde, and 40 grains of sulphonal; the hope being that the paraldehyde would act even before the oils, and that some of the sulphonal would begin taking effect before being expelled by the patient. The author never gave large doses to a constipated patient without purging; but, when the bowels were acting freely, he did not hesitate to give 40 grains whenever he thought it necessary, though he does not remember to have given that dose twice in the twenty-four hours. Six hours later he begins 20-grain doses of sulphonal alone, three times a day, gradually decreasing the dose as opportunity offered. He generally prefers three doses of 20 grains to two of 30, except in tube cases. Little tube feeding will be necessary if hypnotics are properly used.

He has not had to resort to large doses of any hypnotic

since learning the powers and virtues of hyoscine; and since he uses this drug in doses up to $1/50$ of a grain. The usually stated doses of hyoscine— $1/200$ and $1/75$ of a grain—are of no use, he says, in acute insanity, and at least a $1/50$ grain should be given under the skin, or $1/30$ grain by the mouth or hypodermically. If there is any risk attached to its use it is a risk that ought to be run, for the danger of the drug is in any case not so great as the danger of allowing the patient to die of exhaustion. It should be given an extended trial in acute delirious mania and in delirium tremens.

Luminal Febrile Exanthem. H. Weber⁷ describes two cases of luminal exanthem with angina and fever ending in desquamation that occurred in young epileptics who were under luminal treatment receiving 0.050 to 0.10 gm. luminal five times daily. The differential diagnosis from scarlet fever was made on the strength of the atypical fever curve, the slight change in pulse rate, the general feeling of well-being, absence of characteristic changes of the tongue, absence of albumin in the urine, and a leukopenia rather than a leukocytosis.

H. Strauss⁸ also refers to this exanthem following luminal and nirvanol in some of which bloody diarrhea and albuminuria were also observed. He suggests that the condition might be due to anaphylaxis.

Luminal Poisoning Simulating Epidemic Encephalitis. The case of a woman who was given 5 grains of luminal every night for six nights without any results until after the fifth dose had been taken is reported by George Wilson.⁹ On the afternoon of the sixth day, and before she had had the last dose of luminal, she complained of headache and double vision. Her temperature at that time was 100° F. Following the last dose of luminal, the woman went to sleep and remained in a stupor for six days. During this period she could be aroused only to fall again into a state of lethargy; she would stop talking in the middle of a conversation and had to be prodded to keep on chewing when she had a

(7) Therap. Halbmonatsh., Aug. 1, 1921.

(8) Ibid., Feb. 15, 1921.

(9) New York Med. Jour., Oct. 19, 1921.

mouthful of food. She complained of extreme weakness, was unable to hold her head erect, and was scarcely able to raise her hand to her mouth.

“The appearance of the woman’s face suggested a double third nerve weakness; the upper lids could be only partially elevated and the muscles of the forehead assisted in the action. The pupils were moderately dilated and reacted poorly to light. The face was smoothed out. The speech was indistinct and resembled to some extent that of general paresis. A universal hypotonia with a profound depression of the deep reflexes was noted; the plantar and abdominal reflexes were present and normal. The blood, urine, cerebrospinal fluid and eye-grounds were normal. The temperature did not go higher than 99° F., except on the one occasion mentioned above. For six days the woman was in a state of extreme lethargy. At the end of that time she gradually became brighter mentally, although she still continued to sleep a great part of the time. An alarming asthenia persisted for two more weeks, and was so severe that she could not hold her head erect for any length of time. She eventually made a complete recovery.”

ANALGESICS

Indications and Contraindications to Morphine in Neurology and Psychiatry. Alexander Pilez¹⁰ wishes us to keep the fact in mind that opium and its derivatives are quite ineffective against psychomotor excitement and particularly against spasmodic conditions in the ordinary doses. We see, for instance, that morphine injections are administered in attacks of cumulative epilepsy, whether genuine or in paralytics. Here, this drug is not only not indicated but is directly contraindicated. We have at command more effective drugs to combat these attacks, in amylene hydrate, neuronal, and luminal, and possibly lumbar injections.

Morphine is also useless, though perhaps not downright injurious, in the combating of excitement in the mentally affected, in maniacs for instance. In cases in

which packing or continuous baths are impossible, scopolamine in doses of from 0.0005 to 0.001 gm. is suitable. Morphine, further, is absolutely contraindicated in conditions of excitement of the so-called delirium acutum and of delirium tremens. It is completely ineffective against the psychomotor excitement and absolute sleeplessness of these patients. The mortality of this psychosis fluctuates between 10 and 35 per cent. in the clinics where opium and chloral are recommended. The mortality is 3.63 per cent. in cases complicated by somatic affections, and 0.9 per cent. in cases without complications, when the rules of treatment are alcohol as a specific excitant in case of symptoms of heart weakness, *no* hypnotic, and thorough evacuation of the intestinal tract.

Essential sleeplessness, not caused by pain or terror, offers no indication for morphine. In these cases, the numerous actual hypnotics ending in -al, -on, -in, are suitable. Solely in cases of pain and terror, is opium indicated and sovereign in effects. In these cases the actual hypnotics and sedatives fail utterly. At times, in such cases, both morphine and a sleeping dose will have to be combined, in order to avoid the constipating effect of the former. It is well to combine opium with a laxative; for instance, extract of opium and powdered rhubarb root in pills.

With a neuropathic or hysterical patient, morphine should really be only the last resort. Without a compelling reason, the physician ought not to administer morphine subcutaneously, but rather give it by mouth at first. The patient should not know what he is getting. It must be condemned as a serious mistake to give hypodermic syringe and morphine tablets into a patient's own hands. However, if all these conditions are complied with, if the family and personal peculiarities are fully considered, many a physician might be a little more courageous with respect to the administration of morphine where everything else has failed to alleviate the terrible pains of his patient. The author believes that subcutaneous injections of any kind should always be made either in the abdomen or in the back and not

in the arms and legs, the former spots are much less inclined to infiltrations.

Effect of Morphine Upon the Alkali Reserve of the Blood. The well-known respiratory depressant action of morphine and the failure of carbon dioxide to stimulate respiration after morphine has been ascribed to an increase in the alkali reserve of the blood induced by the latter (Hjort and Taylor, 1919). This question has been reinvestigated by H. Gauss¹ with the newer methods for the accurate determination of the alkali reserve in the blood. He found that morphine administered subcutaneously in the form of the sulphate to rabbits, dogs, and sheep, distinctly increased the alkali reserve of the blood plasma of these animals. Likewise, there was a slight but distinct effect upon the P_{H} of the blood plasma. The alkali reserve increase, as the result of the injection of morphine, was greater in rabbits than with dogs or sheep, whether this difference was due to excitement which lessens the alkali reserve of the blood plasma has not been determined. In man, a therapeutic or even a slightly toxic dose (0.015 to 0.030 gm.) of morphine did not have a sufficiently marked effect when administered subcutaneously upon the P_{H} or the alkali reserve of the blood plasma to be demonstrable by present methods of investigation, even though the larger dosage produced well marked respiratory depression with cyanosis. It is possible, of course, that further study may offer conditions suitable for the demonstration in man of an effect analagous to that in animals. At the present time, the respiratory sedative effect of morphine in man can not be explained simply by an action upon the alkali reserve of the blood.

Influence of Morphine in Experimental Septicemia. A. Kraft and N. M. Leitch² undertook an investigation to observe the influence of morphine on the course of septicemia produced by the *Streptococcus hemolyticus*. The strain used was isolated from a case of human septicemia terminating fatally. Rabbits were employed as experimental animals. The authors found that morphine sulphate given in 0.03 gram doses, which is from 1/6 to

(1) Jour. Pharm. and Exper. Therap., January, 1921.

(2) Ibid., June, 1921.

1/10 the fatal dose, lowers the resistance of rabbits toward septicemia. It also lowers the temperature. Hence, in the administration of morphine in infections, the desirable effect,—the sedative action,—should be balanced against the harmful influence of morphine on the course of infection, which is probably due to a number of factors, such as inhibition of phagocytosis, increase in intestinal stasis, with the increased production of toxins, and a general depression of the body temperature, of metabolism and of body defense.

Morphine Respiratory Depression Antagonized by Tyramine. H. G. Barbour and L. L. Maurer³ after having demonstrated by experiments on rats that tyramine acts as a respiratory stimulant increasing the average maximum volume of respired air to 25 per cent. above the normal, studied the question of whether the respiratory depression produced by morphine can be antagonized by tyramine. They found that such antagonism exists and that the most complete antagonism occurs when 1 mg. of morphine is combined with 6 mg. or more of tyramine.

These effects can best be shown by making the animal breathe from 7 to 8 per cent. carbon dioxide which increases the respiratory volume by about one-third in the normal; but fails to do so in the morphinized rat. When tyramine is administered with morphine the usual effect of carbon dioxide upon the breathing is obtained.

The authors have reason to think that the morphine analgesia is not antagonized by tyramine in doses sufficient completely to antagonize the respiratory depression produced by morphine. Hence, this combination might be of value whenever we desire to obtain the morphine analgesia without the tendency of morphine asphyxia as, for instance, in the obstetrical use of morphine, in which the tyramine might serve as a preventive of asphyxia of the new-born. This combination might also be useful [or dangerous—Ed.] in obstetrics because of the stimulant—ergot-like—effect of tyramine upon the uterus. Tyramine might also serve as an antagonist to morphine poisoning.

(3) Jour. Pharm. and Exper. Therap., June, 1920.

Epinephrine as Antidote to Morphine. Having demonstrated by experiments upon human beings that atropine, even in large doses, has no effect upon pulmonary ventilation, A. Bornstein⁴ calls attention to the very effective stimulation of respiration following the administration of from 0.7 to 0.8 mg. of epinephrine in artificial morphine poisoning.

Dover's Powder Improved. K. Kottman⁵ believes that a mixture of emetine with the total alkaloids of opium yields a product of uniform and constant composition and action, which could not but be an improvement over the old fashioned Dover's powder. He believes that emetine is the essential expectoration-favoring ingredient of ipecac and that its action is not dependent upon the nauseant or emetic action. The difference between the emetic and expectorant dose of cephaëline is much less than in case of emetine. Because of this, and also because of the inconstancy of the composition of ipecac, he considers the use of emetine as an expectorant much more rational than the employment of ipecac. The effect hoped for from the emetine is a thinning of the bronchial secretion. This secretion is normally a thin fluid easily propelled by the ciliae of the bronchial mucous membrane. When this fluid becomes viscid by reason of inflammatory changes in the mucous membrane, the ciliae can not propel it, nor is cough usually of much effect in the expectoration of such material. The strain which accompanies coughing and the congestion produced thereby may actually increase the damage. What is needed is to thin the secretion so that the ciliae can propel it. Then the cough is unnecessary. The author believes that this is the philosophy of the addition of opium to ipecac. It not only antagonizes the undesirable cough but also the undesirable by-effects of emetine such as stimulation of the respiratory center and of the vomiting center. By using the total alkaloids of opium instead of the crude opium one obtains a pharmaceutically superior product. The author considers it desirable to use a somewhat larger proportion

(4) Deutsch. med. Wochenschr., 1921, p. 647.

(5) Schweitzer med., Korrespondenz 61, May 5, 1921.

of emetine in the mixture than would be suggested by the composition of the old fashioned Dover's powder.

[Unfortunately, the author does not see fit to give the exact formula of the combination he has found best, but uses his study of Dover's powder, which, as he says, was undertaken at the request of a manufacturer of chemicals, to originate a proprietary medicament under the name of "Ipecopan." There is no reason why a physician might not prescribe a mixture of emetine in proper dosage (5 to 10 mg.) with the addition of one of the ordinary preparations of opium. The chief objection to the non-alkaloidal constituents of opium is that they render it unsuitable for hypodermic use. But inasmuch as this combination is to be taken by mouth the real reason for a pure mixture of opium alkaloids falls to the ground.

From a clinical standpoint it might be admitted that a single dose or at most a few doses of Dover's powder or a modification of it might be useful in the dry stage of an acute bronchitis. But its continuance is certainly contraindicated as soon as the stage of secretion has set in. Opiates should never be used, when there is any danger that the suppression of cough may favor retention of secretion in the chest.—ED.]

Cinchophen, Neocinchophen and Novaspirin in Rheumatic Fever. P. J. Hanzlik, R. W. Scott, C. M. Weidenthal and Joseph Fetterman⁶ gave these drugs to patients with rheumatic fever, until definite effects, or symptoms of drug action, occurred. Then the medication was stopped; and, if no relief was obtained, a full therapeutic (toxic) dose of sodium salicylate as the standard was administered in the usual way. The criteria of complete relief consisted of a sustained fall and return of temperature to normal, prompt disappearance of swelling, redness and pain in the joints, and a sense of well-being. Small doses will give partial and temporary relief in acute rheumatic fever, but the condition demands massive doses in order to obtain complete and lasting relief.

The data indicate that novaspirin is worthless in rheumatic fever. This is due to the inadequate concentra-

(6) Jour. Amer. Med. Ass'n., June 18, 1921.

tion of salicyl in the tissues, which is due in turn to the relative insolubility of the compound and poor absorption from insufficient liberation of salicyl from it in the alimentary tract. The use of novaspirin in the place of the more soluble and absorbable and therapeutically also more effective sodium salicylate is irrational.

Cinchophen gave partial relief from symptoms in rheumatic fever in doses of from 3 to 6 gm., and complete relief in doses of from 10 to 13 gm., while neocinchophen required a somewhat higher range of dosage, namely, from 3 to 8 gm. for partial, and from 11 to 16 gm. for complete relief. Such doses produce characteristic symptoms of salicylism which, however, are less pronounced than those caused by corresponding doses of salicylate. Cinchophen differs from salicylate by causing epigastric pain owing, presumably, to local irritation by the drug. Pain in the epigastrium was absent after large doses of neocinchophen, presumably because of its relatively low solubility in water and weak alkalies, possibly also because it is an ester. Large doses of cinchophen and neocinchophen produced cardiac slowing due to a direct depressant action on the circulation. Cinchophen is injurious to the kidney, as indicated by the occurrence of albuminuria, and sometimes casts and white blood corpuscles, and a diminution in the excretion of phenolsulphonephthalein. Neocinchophen is variable in these effects, albuminuria and a diminution in the excretion of phenolsulphonephthalein occurring in about 50 per cent. of the nine individuals who were observed. As compared with salicylate, cinchophen appears to be about equally efficient, while neocinchophen is somewhat less efficient, as judged by the dosage necessary for therapeutic relief in rheumatic fever. The symptoms of "toxicity" are about the same and renal injury somewhat less after cinchophen, and both the "toxicity" and the renal injury are less pronounced after neocinchophen than after salicylate in corresponding doses.

Cinchophen in Infectious Arthritis. As a result of their chemical and clinical studies, A. F. Chace, V. C. Myers, and J. A. Killian⁷ believe that cinchophen and neocinchophen, particularly the latter, are very promis-

(7) Jour. Amer. Med. Ass'n., Oct. 15, 1921.

ing agents in the treatment of acute infectious arthritis. They point out that the salicylate and cinchophen groups of drugs show comparatively little difference in their analgesic, antipyretic, and "uric-acid eliminating" effects. These drugs also stimulate, to a lesser degree, the elimination of other waste products. There appears to be no relation between their therapeutic efficiency in infectious arthritis and their influence on the blood uric acid. Cinchophen and neocinchophen, in doses of from 50 to 100 grains daily, seemed to have a more specific effect in the severe cases of infectious arthritis, acting in smaller doses, than the salicylates which have the distinct disadvantage of producing proteinuria and casts when given in large doses. On this account, cinchophen and neocinchophen are the drugs of choice when, for any reason, it seems desirable to favor the kidneys. On the other hand, the salicylates have the advantage of being better assimilated by rectum. Cinchophen and neocinchophen, particularly when given with alkalis, are better tolerated by the stomach than salicylates. Since neocinchophen is an ester instead of an acid, there is less need of using an alkali than with cinchophen. In fact, when given without alkali, neocinchophen does not seem to irritate the stomach. Although a few cases of marked idiosyncrasy to the salicylates (acetylsalicylic acid), in the nature of an allergic reaction, have been reported, experience was that patients are more liable to have vasomotor disturbances of the urticarial type from the cinchophen. No serious instances of the latter have been observed.

The Intravenous Administration of Calcium Acetylsalicylate. On the strength of the supposition generally held that the analgesic action of acetylsalicylic acid is due to the unchanged drug, Archibald Campbell⁸ employed intravenous injection of the calcium compound dissolved in water, one part in six. (Messrs. Martindale supply it under the name tylcalsin in 0.5 gram compressed tablets made without the use of wax or theobroma.) He believes that intravenous injection of calcium acetylsalicylate produces a greater and more immediate relief of pain than aspirin given by the mouth, and

(8) Brit. Med. Jour., July 9, 1921.

that its administration is not harmful. It will act beneficially in many cases in which other remedies have failed, and it can be repeated daily.

Campbell has now treated a diversity of painful conditions, including sciatica, acute rheumatism, tabes dorsalis, interstitial keratitis, acute iritis, gonorrhoeal synovitis, arsenical neuritis, dysmenorrhoea, and severe headache of doubtful causation, in all fifty-five cases. Pain is relieved in from half to three-quarters of an hour and the effect persists for several hours, and in some cases for days. In one case of acute rheumatism the patient was unable to take sodium salicylate and aspirin by the mouth on account of gastric irritation. Daily injections of 1 gram of calcium acetylsalicylate produced complete freedom from pain for about six hours. For adults the dose usually given is 1 gram.

The technique is simple: a 1-gram tablet is dissolved in 10 c.c. of distilled water by boiling in a test tube in order to ensure sterilization. The solution is then cooled, and injected into the vein with a glass syringe. It is advisable to inject slowly to allow the solution to mix gradually with the blood stream in order to prevent thrombosis.

MISCELLANEOUS REMEDIES

Atropine in Coryza.⁹ It is stated that checking of the nasal discharge may at times be secured by the prompt application of atropine solution either by introduction into the nose of a pledget of cotton saturated with the solution, or else by repeated irrigation of the nose. This treatment may have to be continued for one and one-half days. Concentration according to mode of application, 1:2,000 and 1:20,000.

The Blood-Pressure Reducing Action of Tincture of Garlic. In view of the fact that we are none too well supplied with medicaments that are capable of reducing blood-pressure and that are otherwise harmless, it may be of interest to note the observation by Loepe and Debray,¹ who found that garlic possesses such virtues.

(9) Therap. Halbmonatsb., July 1, 1921.

(1) Prog. méd., Aug. 20, 1921.

As is the case with other such remedies, it is more effective in patients with high blood-pressure than in those whose blood-pressure is normal. The fall in blood-pressure generally occurs after from thirty to forty-five minutes, occasionally not until an hour and a half, and it usually lasts for a day. The dose of the 10 to 20 per cent. tincture made with 95 per cent. alcohol, is from 15 to 30 minims once or twice daily. The author has not seen any unfavorable results following this treatment.

TOXICOLOGY

Treatment of Poisoning. L. Cheinisse² gives, in a nutshell, the modern treatment of poisoning. Thorough and repeated washing of the stomach, using from 0.5 to 0.75 of a liter of water each time and repeating until perhaps 20 liters have been employed, is the mainstay of treatment; and much superior to emetics. This is followed by the introduction of 2 tablespoonsful of finely powdered charcoal and either 30 gm. of magnesium sulphate or, perhaps better, [in case of all but oil-soluble poisons—Ed.] castor oil. This may be administered in 0.5 liter of water before the tube is withdrawn. Lavage may prove useful even from six to twelve hours after certain poisons have been taken. If too late for lavage, the charcoal and cathartic should be administered. Acids and alkalis, of course, require appropriate antidotes, such as magnesia or dilute acetic acid. Otherwise, charcoal is the best antidote to rely on.

ARSENIC

Chronic Arsenic Poisoning. Ralph Stockman³ records cases in which poisoning occurred from the following amounts of arsenious acid in grains taken for therapeutic purposes: 298, 139, 31, 209, 17½, 6, 50, 4%, 7½, 200, 32⁷/₁₀, 11½. The degrees of poisoning in these cases were very far from being proportional to the dosage. The chief effects were manifested on the skin and the peripheral nerves. The skin becomes of a uni-

(2) *Press. méd.*, Nov. 27, 1920.

(3) *Edinburgh Med. Jour.*, July, 1921.

form or mottled grey color or of a light or dark shade of brown, owing to a granular deposit of pigment; and keratosis takes place on the thick portions of the soles of the feet, much less frequently on the palms of the hands and at other parts (Plate II). The pigmentation most commonly begins on the lower abdomen toward the flanks (Plate III), whence it spreads over the trunk, round the back of the neck, and down the thighs and upper arms, ultimately, in some few cases, involving the whole body. Hyperemia, branny desquamation, and warts are not uncommon; and the nails are sometimes rough and hypertrophied. *Liquor arsenicalis* is frequently added to bromide mixtures with the idea that it prevents bromide acne. It does not do so, however, as the two drugs act on quite different elements of the skin; and it may lead to arsenical poisoning, as in cases reported by the author.

Multiple peripheral neuritis, with all its typical motor, sensory, and trophic disturbances, is the other outstanding feature seen clinically. More or less motor paralysis, increased or absent knee-jerks, atrophy of muscles, tremor, hyperesthesia, numbness, pins and needles, neuralgic pains, herpes along the course of nerves, glossy skin, falling out of hair, and excessive local sweating are some of the more prominent symptoms. Suffusion and redness of the conjunctiva, with itching of the eyelids, and pain in the stomach, are other common occurrences; but these are seen at the beginning of the administration and pass off usually in a few days, often without any stopping of the arsenic.

Stockman concludes that the administration of arsenic compounds may be safely continued for a considerable period after pigmentation of the skin and keratosis have developed. If slight, these clear off rapidly after the administration is stopped, and seem to leave no ill effects. Very deep pigmentation must be avoided, as it may be permanent; and in a few cases the development of cancer has been noted, apparently following upon local irritation. On the other hand, its administration should be stopped at once as soon as the slightest signs of neuritis appear. The lesion is always tedious and troublesome to get rid of, and in some cases is permanent.

LEAD

Lead Poisoning. As a result of his experience, Marvin D. Shie⁴ believes that certain signs and symptoms of plumbism have been given somewhat more importance as diagnostic points than they deserve. Thus, pronounced anemia is present in relatively few cases. The pallor usually present is due to some other cause—possibly a constriction of the peripheral blood-vessels. Basophilic degeneration of the red cells is rare in chronic cases; and its value as a diagnostic point, even in acute cases, has probably been overrated. The presence of hypertonus is extremely variable, though it is nearly always present during attacks of colic. Although constipation is usual, it is not invariably present. Many cases of plumbism—especially acute cases—occur without constipation. The presence of a lead line is also extremely variable. It varies from 90 per cent. to not more than 20 per cent. of different series of cases. A point of diagnostic value is the almost invariable presence of mononucleosis in chronic cases.

BORAX

Fatal Borax Poisoning. Caryl Potter⁵ reports a fatal case of poisoning from perhaps an ounce of borax taken by a man aged 66 at 8 a. m. by mistake instead of a proprietary saline cathartic. Within fifteen minutes he was seized with violent epigastric cramps, accompanied by attacks of retching and vomiting, coming on at from five to ten minute intervals. At 10:15 a. m., the patient's pulse was weak, the extremities cold and clammy, there was cold sweat on the forehead and cyanosis. At intervals of a few minutes he would cry out with pain in the epigastrium and then immediately after he would grasp his throat and complain of difficulty in swallowing, of choking and strangling. Notwithstanding active, hypodermic stimulation (0.003 gm. of strychnine and 2.0 c.c. of camphor in oil), he died in one of these paroxysms about 11 o'clock. Necropsy revealed nothing abnormal.

(4) Jour. Amer. Med. Ass'n., March 26, 1921.

(5) Ibid., Feb. 5, 1921.

TOBACCO

The Effect of Tobacco. W. J. Gies, M. Kahn, and O. Limerick⁶ consider tobacco much more beneficial than harmful to the human race. They point out that as used by those habituated the effect of tobacco is chiefly confined to the vascular and psychic mechanisms. The immediate effect is a moderate but temporary rise in blood-pressure and an increase in the power of concentration, in consequence of a better adjustment of the ego to its environment. The rise in blood-pressure, which is so frequently stressed by those laymen who condemn the use of tobacco, does not exceed in degree or duration that which ordinarily follows a cold bath or sponge; it rarely ever equals that caused by such wholesome pastimes as dancing.

The sequence of the potency of the different forms in which tobacco is generally used runs as follows, in the order of greatest degree to least: Chewing, smoking pipe, smoking cigar, smoking cigarette. It can thus be seen, that, contrary to the prevailing belief among laymen, the cigarette is in fact the least harmful form in which it is possible to use tobacco habitually. There is not the slightest foundation for the popular notion that the paper or the tobacco used in the manufacture of the cigarette contains any substance that is especially injurious to the human organism.

Man learned by chance that tobacco (after having once set in operation the specific antidotal mechanism of the body) gives rise to certain pleasurable sensations; that it allays restlessness, tranquilizes emotional inquietude and fosters repose. Profiting by experience, he in time came to resort to tobacco whenever he felt the need of relief from physical or emotional strain. It is an impulse acquired under the influence of selective palliation. It varies in intensity and frequency of recurrence, according to the degree of individual ill adjustment to environment. It is, as a rule, moderate in those fairly well-adjusted to external conditions of life, and immoderate in those less fortunately circumstanced. After breaking the habit of tobacco smoking, the desire for the plant

(6) New York Med. Jour., June 1, 1921.

does not have any cumulative physiologic force of the specific craving for such habit-forming drugs as morphine. The tobacco habit is not a drug habit in the sense in which the term is commonly understood. The toxic effects of tobacco on the user of the plant are relatively slight and only local at most. Tobacco does not cause disease of mind or body. The authors believe that the condition commonly termed smoker's heart is often due to endocarditis associated with gonorrhea, syphilis, rheumatism, tonsillitis, pyorrhea alveolaris, dental abscesses, and other causes. They do, however, admit that the excessive use of tobacco may prove harmful in certain neurovascular disorders, and that the habitual use of tobacco by juveniles is harmful.

ALCOHOL

Alcohol and Caffeine Compared. H. L. Hollingworth⁷ reports results of a painstaking experiment conducted with alcohol given in the form of 2.75 per cent. beer to six adult males, who ranged in age from 21 to 29 years, and who gave their whole time for a period of two weeks to the experiment. The dose was taken practically on an empty stomach at the usual lunch hour. Six tests of

| TEST | Blank Days. | Control Days. | Dinner Day. | Alcohol 40-50 Cc. | Doses 66-79 Cc. | Caffeine 3-4 gr. | Doses 6 gr. |
|--------------------|-------------|---------------|-------------|-------------------|-----------------|------------------|-------------|
| Pulse-rate..... | -7 | 0 | 24 | 8 | 10 | ... | ... |
| Steadiness..... | 11 | -21 | -61 | -68 | -241 | -2 | -583 |
| Tapping..... | -2 | 0 | 8 | -7 | -13 | 3 | 4 |
| Co-ordination..... | 3 | -2 | -2 | -6 | -10 | 0 | -4 |
| Color naming..... | -6 | -3 | 8 | -2 | -7 | 7 | 4 |
| Opposites..... | -2 | -7 | 5 | -5 | -12 | 5 | 6 |
| Adding..... | -4 | 0 | 5 | -10 | -15 | 2 | 3 |

each type of process preceded the dose in the forenoon, and six tests followed the dose in the afternoon. On certain days a "control" dose was given, which was identical in all respects with the standard beer except for the removal of its alcoholic content. On one day, instead of alcohol or control doses, a heavy midday meal was given. The results of these tests are compared in the accompanying table with those of a previous study in which the same technique was used to determine the

(7) Therap. Gazette, February, 1921.

effects of caffeine: In this table a minus sign indicates a loss of efficiency, or at least a decrease in the score or rate. The figure in each case is percentage of forenoon efficiency, either gained or lost in the afternoon. It will be noted that the effects of alcohol and caffeine are in general dissimilar in direction. The alcohol invariably produces lower scores, the caffeine higher scores, excepting as regards "steadiness" measured by tremor, which is even more increased by large doses of caffeine (the amount contained in two ordinary cups of coffee) and "coördination," measured by number of bulls-eye strokes with hand stylus. These results represent averages of the six subject's records. All the individuals consistently gave the same type of effect from alcohol, but they differed definitely among themselves in the degree of this effect. Two of the individuals were very susceptible, showing in all or nearly all tests effects from both small and large doses. Two individuals on the other hand showed effects only after the larger doses. The remaining two individuals stood midway between these two pairs. The study of this idiosyncrasy yields a number of definite points of interest, which may be summed up as follows:

1. Idiosyncrasy does not vary with age, initial pulse, or previous alcohol habits.
2. Susceptibility to alcohol varies inversely with height, weight, and habits of regular and active exercise.
3. Susceptibility varies inversely with general competence. Those who are able to do superior work in the tests in general are less susceptible than those whose final achievement in the tests is relatively inferior.
4. Susceptibility varies inversely with capacity to improve as the result of practice. Good learners are less influenced than are poor learners.
5. Susceptibility to effects of alcohol in performance in the tests is inversely related to the effects of alcohol on pulse rate. Those who are most affected in their work show least change of pulse rate. Those whose pulse rate is most conspicuously changed by alcohol show least effect in their work.

[These results are of more than ordinary importance in these days, when the liquor interests, in their final

life and death struggle, make use of every possible subterfuge or vantage ground to hamper or annul the operation of the prohibition amendment. The plea is made that the consumption of light wines and beers should be permitted, as they are harmless and non-intoxicating. Hollingworth's results show that, even in this high dilution, alcohol demonstrates its action as a cerebral depressant in an unmistakable manner. Caffeine, on the other hand, is shown to be a cerebral stimulant, the degree of its effect being greater than indicated by the figure in the last two columns of the table when it is added to the natural depression that occurs in the afternoon of the blank days, shown in column one. The caffeine effect, it will be noticed, is strictly comparable to that of a heavy midday meal. The well-known "tremulousness" of those who use caffeine to excess, is also well-shown by these experiments.—Ed.]

Relative Toxicity of Ethyl, Methyl and "Wood" Alcohols. While actual experience with cases of human poisoning have shown methyl and "wood" alcohol to be more toxic than ethyl alcohol, a curious experimental observation, known as Richardson's Law (1869), is recorded in books on pharmacology which is to the effect that "the toxicity of the alcohols belonging to the fatty series is in proportion to their molecular weight." That is, that methyl alcohol is less toxic than ethyl alcohol. This "law" has been confirmed and amplified by experiments of numerous later observers, most recently by D. I. Macht,⁸ who found that the toxicity of the normal alcohols—methyl, ethyl, butyl, and amyl—increases with their place in the aliphatic series, as indicated by the lethal dosage for cats, and by their effects on isolated frog's heart and plain muscle preparations.

This apparent contradiction between clinical experience and laboratory experiment is cleared up when we make a sharp distinction between the acute or immediate, and the secondary or remote effects of the drugs, as is well illustrated by the studies of chronic intoxications on albino rats by Torald Sollmann,⁹ who showed by carefully controlled feeding experiments in which the alco-

(8) Jour. Pharm. and Exper. Therap., August, 1920.

(9) Ibid., November, 1920.

PLATE II.



Stockman's Case I. The skin on the back of the hands was very coarse, the nails were very irregular and rough, with a ragged thickened matrix projecting at the free ends.—Stockman, page 184.



Stockman's Case I. Woman, aged 49, who had for over six years taken thrice daily, on account of nervous excitability, a mixture of bromides with 5 minims liquor arsenicalis, in each dose. Fig. 1 showing rough, irregular keratosis of the soles of the feet.

PLATE III.



Stockman's Case I showing the deep mottled greyish-brown pigmentation of the whole trunk, neck, thighs, and upper arms, much lighter pigmentation of the forearms and legs.—Stockman, page 184.

hols were added to the drinking water that methyl alcohol is much more toxic than ethyl alcohol. It was found that the continuous consumption by rats of ethyl alcohol in dose of 2.7 to 9.4 c.c. per day (corresponding to 160 to 560 c.c. for a 60 kg. man.) interferes considerably with their growth and diminishes the consumption of food, though little or no mortality occurs after periods of months. Methyl and "wood" alcohols, 3.4 c.c. per kg. per day of 5 per cent. solution (equal to 200 c.c. for a 60 kg. man) produced much greater loss of weight, great diminution in the consumption of food and drink, and caused death within a few weeks. "Wood" alcohol was found rather less toxic than pure methyl alcohol, but more deleterious than ethyl alcohol even when the latter is given in three times the dosage. This investigation brings out the deleterious effects of chronic alcoholism on growth; and emphasizes that the dangers of chronic alcoholism are much greater with methyl alcohol than with ethyl alcohol. It proves that the "impurities" of wood alcohol play only a minor part in chronic intoxication, the methyl alcohol itself being the dominant toxic agent.

[The reason for the greater toxicity of methyl alcohol must, in view of these facts, lie in secondary products formed by oxidation of the alcohol in the system. Two oxidation products chiefly have been incriminated: formaldehyde and formic acid. That the latter is probably of little importance in this connection is shown by Sollmann's feeding experiments in which he compared the toxicity of formic acid with that of acetic acid (next article) and found both equally harmless.—Ed.]

MISCELLANEOUS POISONS

Acetic and Formic Acid Toxicity. Torald Sollmann¹ investigated, by means of feeding experiments on albino rats, the question of the relative safety of acetic acid and formic acid when supplied to animals in concentrations up to 0.5 per cent. and in daily doses up to 0.36 c.c. per kg. of body weight for from two to four months, this being the sole source of fluid for the animals. The

(1) Jour. Pharm. and Exper. Therap., January, 1921.

occasion for the experiment was the question of the use of formic acid as a preservative in foods. The supposed safety of acetic acid for similar purposes made this an admirable measure of comparison. These experiments also presented an opportunity to study the effects of the continued use of acetic acid which had not previously been determined. It was found that concentrations up to 0.25 per cent. corresponding to a daily dose of 0.2 c.c. of acid per kg. of body weight, produced no effect on general appetite or consumption of fluid. Both are therefore quite harmless.

Concentrations of 0.5 per cent and daily doses up to 0.36 c.c. of either acid per kg. of body weight for from two to four months, lessened materially, immediately and progressively the appetite and growth but not the fluid consumption. This is evidently due to their acidity; but the experiments do not throw any light as to whether this is due to local action on digestion, or whether to some more profound disturbance of the acid-base equilibrium.

Acute Nitrobenzol Poisoning. R. F. Loeb, A. V. Bock and R. Fitz² report the cases of two young men, who during a drinking party, partook freely of Jamaica ginger containing a high percentage of nitrobenzol. After an interval of about three hours, there appeared generalized headache, nausea, blurring of vision, dizziness and more or less loss of consciousness. The color of the skin was steel grey-blue, due to loss of the oxygen transporting function of the blood. It is not certain whether nitrobenzol-hemoglobin, methemoglobin, or both are formed. The changed hemoglobin, as a rule, returns to normal hemoglobin quickly. There was found no change in the total amount of hemoglobin or total number of red cells while the oxygen capacity of the blood was remarkably diminished—to about one-third of the normal venous blood capacity.

No urine was excreted for six hours. The urine then passed was almost black in color and contained para-amido-phenol. In the more severe case on the third day the excretion rate as tested by phenolsulphonephthalein was only 20 per cent. in two hours.

There is no specific antidotal treatment. Bleeding and transfusion seem logical therapeutic procedures for the most severe cases. In the two cases reported rapid recovery occurred after withdrawal of 100 c.c. of blood and transfusion of 600 c.c. of normal blood—the patient suddenly woke up in the middle of the transfusion. A mild uncomplicated pneumonia followed in one case; the other patient recovered entirely in a day.

The Therapeutics of Narcotism. Alexander Lambert³ asserts that the chief difficulty in the treatment of narcotism is that of the cause, for the underlying causes which force man to seek forgetfulness are as varied as the causes of pain or of wounded personality. The care of the narcotic addict, to be successful, must be the solution of an individual variation of a general problem, and not the routine dealing with a mass of humanity poisoned by the same intoxicant. When we have tided over the patient for the few days necessary to remove from him the urgent physical necessity of the habitual taking of his drug, when we have successfully unpoisoned him, from his particular narcotic, the real treatment has only begun. He must now be built up and regenerated in body and mind.

To unpoison the patient of his drugs—and during the first few days of his convalescence he should be kept quiet—often it is wise to keep him in bed. The ambulatory treatment has nearly always proved a delusion and a failure. The vast majority of human beings are, unaided, utterly unable to free themselves from the grip of the narcotic addiction; and the treatment by ambulatory self-reduction is, in the enormous majority of patients, doomed to certain failure. All users of narcotics, take more than they need to produce the desired effect. Hence, in the majority of patients we can cut down the amount of narcotic taken to one-half in twenty-four hours without the symptoms of withdrawal occurring. In the following twenty-four hours one may often again cut down half the dose, and this again without withdrawal symptoms, but there comes a time when the slightest reduction of the amount given brings on the suffering. If the patients have confidence that they will

(3) *Therap. Gazette*, December, 1920.

receive the required amount to make them comfortable, they can be cut down much further than if they are in doubt or fear. Hence, no man can successfully deal with narcotic addicts unless he can gain their confidence, and unless he is willing to meet them more than half-way and tell them the truth.

For assistance during the acute stage of unpoisoning from the narcotic we have three chief drugs: First, scopolamine; secondly, belladonna, and thirdly, eserine and pilocarpine. Some method of unpoisoning the patient from his drug is an absolute essential to any intelligent care of him. A poisoned personality can not be rebuilt and regenerated until it is unpoisoned. The principles on which the belladonna treatment rests are the reduction of the narcotic in a few days, and during this period of reduction an hourly administration day and night of a mixture of belladonna, hyoscyamine, and xanthoxylon. The symptoms guiding the increase or diminution of this belladonna mixture are those of beginning evidences of intoxication from belladonna—that is, the dry mouth, the dilated pupils, or the red, dry throat, or the red, dry, hot skin. The belladonna must be pushed up to but not beyond physiologic tolerance, and so long as this physiologic limit is reached it matters not how much or how little belladonna is used. Most patients who have taken opium or one of its tinctures or morphine for a long period of time require very vigorous catharsis during this treatment. This treatment is applicable for all kinds of narcotics; and, in the end, when successfully carried out—that is, after four or five days—it does obliterate the craving for the narcotic.

In the scopolamine treatment patients are thoroughly purged before beginning the treatment, and after a final dose of their narcotic, as soon as they begin to show signs of discomfort from its lack, they are given doses of scopolamine $\frac{1}{200}$ to $\frac{1}{75}$ of a grain and kept under it in a state of mild delirium and mental anesthesia for about thirty-six or forty-eight hours or longer, the object being to tide them over the usual forty-eight or seventy-two hours of withdrawal symptoms; then they are allowed to come out and begin their convalescence. After this treatment ceases, they usually still feel a craving for

their drug; and the exhaustion and depression from the scopalamine is intense.

The eserine and pilocarpine method of withdrawal is particularly useful in the heroine cases, and in patients who have been taking small doses of morphine for a short time. The patient has the preliminary catharsis and initial dose of about $\frac{1}{2}$ grain of his heroine or his morphine, and he is given hypodermically a $\frac{1}{50}$ of a grain of eserine and a $\frac{1}{15}$ of a grain of pilocarpine. This should be repeated at no longer intervals than two and a half hours. After the first twenty-four hours, the eserine should be discontinued but the pilocarpine kept up, which should be continued for two or three days or longer. The time between each pilocarpine dose should be lengthened toward the end of the treatment. The patient should have each night sufficient cathartic to produce a good result the following day. If during the treatment the patient shows too much restlessness and withdrawal symptoms, he can be quieted with a small dose of morphine from time to time. Care must be taken in the first days that these patients do not over-eat, for they possess a tremendous appetite and over-eating brings back their withdrawal symptoms.

When the narcotic has been taken to cover some physical pain, after-care in convalescence is the most important therapeutic measure of the entire treatment; and, unless sufficiently individualized after-care is given for a sufficient length of time, it is futile and useless to take these individuals off their narcotic and expect the majority to do anything but hurry back to its use. One frequently uncovers disease processes which were unsuspected. At times surgical conditions are discovered for the relief of which nothing but surgery will suffice. If that be so it is well to have this procedure taken quickly, and if it means acute suffering one often has to put the patients back on their morphine to tide them through these surgical procedures, and then afterward they are easily taken off the narcotic.

Cocaine and heroine addicts, who form nearly four-fifths of the narcotic addicts of today, are usually under 30 years of age, frequently feeble-minded, inadequate personalities drifting into the evil practice thoughtlessly.

These need weeks or months of physical upbuilding, of mental reorganization, and moral regeneration. This can best be done through some institutional farm or farm colony by which they can obtain the physical rehabilitation which many of them sadly need. Many are of the criminal type, and our after-care must be modified to meet their individual problems. None of the narcotic addicts with lowered moral tone is ever raised higher than he thinks the physician expects him to go. They are continually seeking for an excuse to sag back to a lower level through moral inertia. The uncompromising vigorous and unceasing appeal to their better natures, coupled with a ready outspoken sympathy for their condition and their endeavors to improve, will pull them up, and hold them up in their reformation. There is a class of the helpless sufferers whose condition is such that neither surgery nor medicine offers any relief, and they must face a life of pain and misery. These patients should not be deprived of the amount of narcotic which will make their existence bearable, and the amount necessary should be accurately judged by the physician.

Some patients do not take a single narcotic; they take heroine and cocaine or morphine and cocaine. Few combine alcohol and morphine, and very few indeed combine alcohol, cocaine and morphine. All patients who are using cocaine should be taken off it immediately, and put on the belladonna treatment, and then their heroine or morphine or whatever other form of narcotic they are taking should be treated as if it were alone the narcotic to be dealt with. In elderly people who are given to morphine and alcohol or any such combination, it is best to take them off their alcohol first, leaving them their morphine, then build up, continuing the small doses of morphine that are necessary to keep them comfortable, and after a few weeks when they are built up bodily and in good condition they can be easily taken off their small and reduced doses of morphine.

Toxicology of Rubber Goods. Walter I. Galland³ influenced by a report from Stokes and Busman (1920), which traces some untoward reactions following arshenamine injections to a certain brand of rubber tubing, conducted an examination of eleven samples of rub-

(3) New York Med. Jour., Feb. 19, 1921.

ber tubing used in two representative institutions in New York. These samples were analyzed for the presence of antimony and lead. He found that all of the red tubes contained antimony and four of these contained lead in addition. The tubes other than red contained neither antimony nor lead, but this point should not be interpreted as meaning that all such tubings are free from toxic substances. It is possible that antimony may at times be dissolved from tubing, by alkaline arsphenamine solutions. The presence of poisonous substances in rubber compounds destined for medical and surgical use is a menace. Rubber compounds can and should be manufactured for surgical use free from deleterious substances.

NON-PHARMACAL THERAPEUTICS

Pleas for Physiotherapy. Joseph Riviere⁴ prefers the word "physiotherapy" to "physiotherapy," as far more precise. Physiotherapy (from Greek "*physis*," meaning Nature), simply means "natural cure," the utilization, by the physician, of all the elements supplied to him by Nature for the treatment of disease. The whole medical art is essentially physiotherapeutic. Do not medicines themselves form part of the domain and the province of nature? Physiotherapy (from Greek, "*physike*," physics) signifies the application to daily therapeutics of all apparatus, instruments and machines which physical science furnishes us.

Perry Marshall⁵ tells the story of a great physician, who was dying and around whom were gathered numerous doctor friends. They wept. The world was to be deprived of so saving a power! None could take his place. He asked them to raise his head on a high pillow. He then began to say, "I leave behind me several physicians greater than myself." They each wondered which of them he would mention. "Is it I?" each thought. Breathlessly they listened as he labored, till he could say, "Rest, exercise, air, warmth and water."

It is a wonderful thing, Marshall says, noting to what an extent *rest* in bed for two or three days, or more,

(4) New York Med. Jour., Dec. 11, 1920.

(5) Amer. Medicine, December, 1920.

will change the aggressive character of colds, gripes, or influenzas, and most febrile diseases, or those threatening to become febrile. Nervous diseases bordering on neurasthenia and hysteria and other forms of nerve-worn conditions are often unamenable to treatment without combining with it rest, from a few days to a few weeks, taking care not to let the mind possess itself of the idea that the bed must become a permanent institution.

In any febrile disease, especially at its beginning, the application of large, heavy towels saturated with hot water, extending from the clavicles to the thighs and reaching well around laterally, is soon followed by the arrest of the rise and often by rapid fall of the fever, especially in ephemeral or grippy cases to a degree not effected by any safe medicine. In many cases of general debility, the morning or evening or both morning and evening tepid bath equals in value any medicinal treatment.

Exercise is one of this world's great therapeutic agents in aid of health where applicable. Marshall has known a weak heart to grow strong, while the muscles were exercised by the axe, chopping wood.

Warmth in colds and grippe is of prime importance. The cough is soothed by the warmth of the bed. Cold treatment is pernicious in influenza. In Springfield, Mass., two years ago in the early fall, when the cold treatment idea was so prevalent for influenza patients, a tent hospital was provided where the victims died so rapidly that it had to be discontinued. Clean air is indeed desirable, but with cold air and especially with cold wind blowing over the patient, what wonder that the patient perished? The tuberculous, on the other hand, must have outdoor air, even if it be cold. His germs are house germs, as some flies are house flies. A few hours in the sunshine destroys them, but indoors they can live long, if not forever.

MECHANOTHERAPY

Mechanotherapy. Mrs. A. Kellgren-Cyriax⁶ pleads for a more extended application of mechanotherapy, and

(6) Practitioner, March, 1921.

for its introduction into medical schools. In mechanotherapy actual harm may be done if we do not understand its fundamental laws. For example:

1. Exercising a contracted muscle, instead of strengthening its weakened antagonist. A good instance of this is the common mistake of exercising the stronger muscles in spinal curvatures, thereby increasing the deformity. Under this heading, too, comes the passive forcible intermittent stretching of a contracted muscle in the hope that it will become elongated.

2. Attempting to mobilize a stiff joint without proper fixation of the joints above it.

3. Permitting joints at a distance from a fracture or other trauma to become stiff or even ankylosed, because it is not realized that these can be exercised without the slightest disturbance of the injured part.

4. Neglecting to apply circulation-promoting movements to areas where wounds can not heal simply from stasis.

5. Applying movements in emphysema which expand the chest instead of those that contract it.

6. Applying abdominal massage intended for the transverse colon in conditions in which from enteroptosis or dilatation the stomach is occupying its place. The result will be massage of the stomach in the wrong direction.

7. Applying powerful active exercises and passive manipulations for constipation which is due to colitis, not to intestinal atony, thereby increasing the amount of inflammation in the colon.

The author then describes "nerve friction" introduced by H. Kellgren, by means of which nerves can be stimulated, also manual "vibration" by means of which they can be soothed.


"The technique of nerve friction to stimulate nerves is briefly as follows: The area in which the nerve lies must be in a state of relaxation and the position of the nerve accurately determined. The hand of the operator is kept with the fingers approximated and somewhat flexed using one finger alone, or the thumb and index in apposition, or several fingers. They are placed at right angles to the long axis of the nerve to be treated

and drawn sharply across it, as if playing upon the strings of a harp. It is of the utmost importance that the finger-tips and the structures between them and the nerve move as one over the latter, otherwise a mere massage of the skin will result. If correctly applied, nerve friction causes a decided feeling of stimulation in the nerve thus treated; if incorrectly applied, an unpleasant dull ache will result." This direct nerve stimulation enables us to influence every muscle and organ in the body, either directly or reflexly.

The technique of vibration used as a sedative is briefly as follows: "Depending upon the size of the area to be treated the operator may use one, two, or more fingers, with or without a portion of the palm of the hand. The joints of the fingers, wrist, and elbow should be kept as loose as possible compatible with the correct execution of the movement, and the metacarpophalangeal and interphalangeal joints should be slightly flexed. A rapid alternating contraction and relaxation of some of the muscles of the forearm in whole or in part is then set up. The amount of muscular force employed should be minimized and so small that the active muscles are in a state of *incomplete* tetanus, not a complete one. During the performance of the vibrations, the fingers must remain in contact with the part treated; they must not leave it, otherwise the manipulation will resolve itself into a fine tapotement. Vibration should never be produced by means of powerful contraction, *i. e.*, complete tetanus, of the whole arm and shoulder." Vibration, such as described, can be kept up by a practiced hand for long periods without undue fatigue. These manual vibrations have a decidedly soothing effect, irrespective of whether they are applied over an actual large nerve trunk or over nerve terminals in an irritated area, large or small, and whether the condition treated is chronic or acute.

We should not have so many "bone setters" and other charlatans if we understood mechanotherapy.

Semisitting Posture for Bed Patient. To make a patient comfortable in a semisitting position in bed, H. Burekhardt⁷ suggests wrapping a blanket around a cane

(7) Münch. med. Wochenschr., March 25, 1921. 

or sawed-off broom handle and fastening it with a safety pin. This roll is then placed crosswise of the bed under the thigh and is kept from slipping down by tying the ends of the cane by means of cords to the head of the bed. The back is supported in the usual manner by a back rest or by pillows.

ELECTROTHERAPY

Some Examples of the Use of Galvanotherapy. Some practical points are brought out by A. R. Friel⁸.

If the cause of pain is at the place where the pain is felt, treatment by the introduction of the salicyl ion is often effective. Thus, a man suffering from a gunshot wound in the leg was relieved of his pain by having his leg placed in a bath of a solution of sodium salicylate in warm water ionized for an hour. This is an illustration of the success to be attained if conditions allow you to get at the spot. The same immediate measure or relief is not to be expected in a case at the other end of the scale, such as sciatica, where thick layers of fat and muscle intervene between the electrode and the inflamed nerve. The more superficial, and therefore the more accessible, the situation we have to treat the more likely we are to be successful.

Many slight injuries and sprains with resultant "thickening" in the neighborhood of the superficial joints, such as knee, fingers, wrist and elbow, often yield to ionization. There is a striking experiment devised by Professor Leduc (Fig. 21) which leads one to believe that in addition to the nutritional changes that occur from the exchange of ions as the result of the current between the cells and the fluid in contact with them, there is also a transfer of water from the positive to the negative side, and an increased solubility of exudates there. Some egg white is introduced into the bend of a U-tube and coagulated by immersion in boiling water. A solution of a salt is then poured into each limb and a current of electricity passed through the tube for some hours. It is then seen that the fluid has sunk on the side connected with the positive pole and risen on the

(8) Practitioner, August, 1921.

negative side; and, moreover, the albumin on the latter side is dissolved. By means of this action, an exudate can often be entirely dissipated. The duration of the application should be long, the current strong, and several sittings may be necessary. It is, on the other hand, unlikely that we can exert such influence on structures deeply placed beneath muscles because of diffusion of the current into other tissues.

Often brilliant results are obtained in the treatment of local sepsis by zinc ionization. The zinc ion is a great coagulant of albumin. It has no selective action

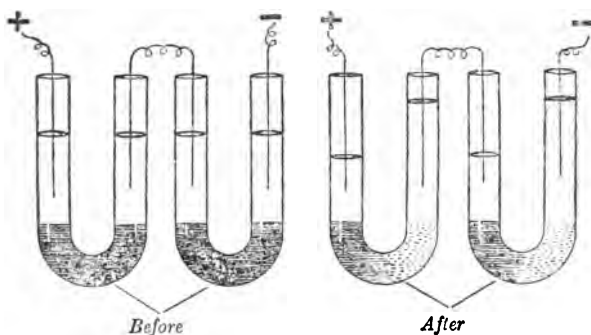


Fig. 21.

on the bacteria. Zinc ionization is a method by which bacteria in an albuminous matrix can be killed. The sharp delimitation between precipitated and unaltered serum explains the absence of irritation of deeper tissues when the surface of an ulcer, for example, is exposed to zinc ionization. Ionization causes deeper penetration, however, than mere application of a lotion. In uncomplicated chronic suppurative otitis we have an "infection of the discharge," deceptively called "mixed infection," which indicates stagnation of the fluid exuded, which in turn means structural or mechanical conditions of the cavity which favor that stagnation. By what is called drainage we deal with the accumulation of considerable—macroscopic—quantities of fluid. We do not deal with the microscopic layer of serum and bacteria adhering to the surface of the tissue. For this, ionization

with zinc is an effective method of treatment. Some attention must be paid to the tissues forming the wall in the choice of dosage. When they consist of mucous membrane covered with epithelium, the dose should be moderate, and moderate doses are effective. When an ear, presenting the conditions described, is examined within twenty-four hours of treatment, it is often found that the suppuration has entirely ceased. The ear is dry, the drum is clean, and the mucous membrane is pale. It is this rapid and complete subsidence of suppuration that serves as a criterion for assessing the value of zinc ionization. However, not every case of chronic otorrhea will show this result. When the mastoid is infected, it is usually not possible to introduce the fluid and distribute the current to the whole of the infected area. Again, the presence of polypi and granulations which exude fluid, which it is impossible to keep sterile because it is in contact with the air, point to the necessity of first getting rid of the polypi and granulations before attempting ionization. Similar conditions occur in other parts of the body besides the ear, *e. g.*, chronic endometritis and pyorrhoea alveolaris. In sinuses and ulcers, the surface is covered, in contrast to what occurs in the ear, with ordinary granulation tissue; in abscesses, with what is called the pyogenic membrane. There is no epithelium, the integrity of which must be respected, forming an efficient barrier between the outside world and the tissues. Consequently, it is quite safe and, indeed, desirable to give a larger dose than in case of the ear.

RADIOTHERAPY

GENERAL USES OF VARIOUS FORMS OF RADIOTHERAPY

Radiotherapy. Robert Knox¹ (2) points out the unity of action of the various radiations. The wave-length of the radiation is the determining factor. The available range of wave-length in radiation treatment starts with the very low penetrative value of the ultra-violet radiation to the extremely penetrating radiations

(1) Edinburgh Med. Jour., May, 1921.

from radium: the Gamma ray representing so far as we know at present the extreme limit of penetration. The limitation of action depending upon the power to penetrate the tissues is the key to the explanation of the effects produced, and it may be taken for granted that radiations of any wave-length will act upon living tissues, provided they are brought into contact with them for a sufficiently long time. Ultra-violet radiation will cause a violent superficial reaction upon the skin. Roentgen rays of long wave-length will give an equally violent reaction if the dose is sufficient, while it is also possible, by a long exposure to the Gamma radiation from radium, to produce a vigorous superficial reaction. When deeper effects are required, it is necessary to resort to the more penetrating radiations, the less penetrating having very little effect beyond a centimeter or so of tissue. In superficial lesions of the skin, ultra-violet rays, x -rays, and radium rays can all be employed with success.

A great deal of unnecessary discussion has taken place on the relative values of x -rays and radium rays, the assumption being that these agents act differently upon the tissues. Given an equal wave-length from either agent the effect will be the same, and sometimes the agents act best in combination. For example, in cancer of the cervix uteri, radium applied directly to the growth gives very brilliant results; these are, however, purely local and not permanent. The use of both agents would appear to be a rational procedure. The radium acting from the local focus and spreading outward to the periphery, while the x -rays are used from the periphery to the central focus point. It is possible that in this way peripheral extension of the new growth may be checked.

Superficial lesions are the most favorable for treatment, in so far as they can be kept continually under observation and the progress be noted. The study of the changes induced in superficial structures gives an indication of the type of case likely to respond to treatment, and the probability of influencing deeper morbid conditions. Simple chronic inflammatory lesions—simple ulcer, nevus, etc.,—can be beneficially treated with re-

markable accuracy; conditions that verge on the malignant, *i. e.*, rodent ulcer and epithelioma, are more intractable; while the very malignant forms of carcinoma frequently resist treatment altogether. Exactly the same sequence is noted in the so-called deep therapy. The effects are, however, much more difficult to obtain on account of the greater difficulty in administering the correct dosage. Knox then gives his experience in various conditions which may be summarized as follows:

Of superficial lesions, tinea of the scalp has been the disease most frequently and most successfully treated. However, in view of the danger of the application, other safer methods should first be given a trial. If, in the early stages, treatment by ointments and disinfectants is efficiently carried out, success should follow. Disastrous results may follow upon *x*-ray treatment of ringworm, even in most competent hands, by a slight error in technique, and, if a disaster occurs, it is likely to be permanent.

Among a large number of cases of rodent ulcers, in several successful cases the patients are still well; but the majority even of the successful cases relapse from time to time and ultimately resist treatment.

In lupus vulgaris, ultra-violet radiation is most useful. Roentgen rays should be used only occasionally, in well-measured doses, care being taken not to over-stimulate the tissues at any time. If due care is exercised very good therapeutic effects ensue. In rebellious acne of the face, a combined attack with drugs, vaccines and practically all wave-lengths of radiations may result in success.

Hyperidrosis is readily controlled by radiations. Several doses of *x*-rays directed toward the affected region will usually produce the desired effect.

In morbid conditions of the blood, the leukemias, Banti's disease, etc., the results obtained are disappointing. Often a very favorable response is obtained, which may persist for many months, even years; but the final result is unfavorable. In the future an improved technique might help to maintain the effects and in time restore the balance in the blood constituents and so effect a cure.

In diseases of the blood in which the spleen is enlarged, as in leukemia and splenic anemia, radiations claim first place with surgery in treatment; and it may be asserted with a fair degree of certainty that the results with the rays may be as good as those obtained with splenectomy. The spleen can be reduced in size, or even returned to the normal by carefully-judged radiation treatment. Doses given at regular intervals after the normal has been achieved may be helpful in keeping in check the ravages of the disease.

In *exophthalmic goiter*, radiation treatment, Knox says, gives excellent results. Acute cases require combined treatment, particularly rest and drugs, extending over long periods of time.

The value of radiation in the treatment of the lymphatic system is unquestioned. The response is so marked that a measured dose might be used as a diagnostic test. Taking this response of enlarged glands to radiation treatment, the following table may be constructed.

(1) *Inflammatory Enlarged Glands*: Very rapid response.

(2) *Lymphadenomatous Glands*: Rapid response.

(3) *Sarcomatous Glands*: Rapid response, but there is a tendency to recurrence, and an ultimate refusal to respond to further treatment.

(4) *Tuberculous Glands*: Slow response. They very rarely disappear; they tend to become active again after longer or shorter intervals. It is therefore well to remove the glands after they have become quiescent.

(5) *Carcinomatous Glands*: Very slow response. They hardly ever disappear or become quiescent; it is better, therefore, to remove them whenever possible even after prolonged radiation treatment.

(6) *Enlarged Glands Due to a Mixed Infection*: These will, at times, behave in a manner which is disconcerting when an attempt is made to classify the type of gland according to the response to treatment, either by drugs or radiations.

While a well-developed uterine fibroid never disappears completely by any method of treatment other than the operative one, it is a common experience to find that there

has been a marked diminution in the size of the tumor under radiotherapy. Very large tumors have diminished to one-half or even one-third of the original. In a fairly large percentage of the cases treated, there may be no diminution in size; but the patients improve greatly in health, because of the arrest of the hemorrhage. In such cases, the question of operation should be seriously considered. It is not surprising that no marked change can be detected in large tumors, especially when they are largely composed of fibrous tissue and are not very vascular. The radiation dose required to influence such tissue would be so enormous that the more superficial tissues of the patient would be seriously damaged. Any improvement obtained in cases of this type must be induced through the action upon the ovaries and the blood-supply generally. On the other hand, it is not wise to assume that because no great diminution in the size of the tumor is brought about, no good is being done. In cases of large inoperable tumors where pressure effects are present or are threatening, great relief may be obtained by a very small reduction in the size of the tumor. This particularly applies to the large tumor filling the pelvis and pressing upon the uterus. As a rule it is the smaller and more active tumor which is most likely to be influenced by radiations. A small tumor may give rise to very great hemorrhage. If the proper dosage is employed the hemorrhage can be arrested, and the arrest may be permanent. Cases in which the hemorrhage recurred have been treated again with a satisfactory result.

Clinical Features as the Determining Factors in the Application of Radium and Roentgen Rays in Malignancy. Paul Eisen² develops the proposition that the one factor which determines the amount of rays to be employed is the condition of the patient himself. Generally speaking, the younger the patient is, the lower is the radiosensibility of the growth. Thus in sarcoma nearly all patients below 30 succumb to the disease. The longer a patient has had a cancer the easier it generally is to attack it. We see this daily in epithelioma of the aged. They are cured of their cancers although they

(2) Jour. Mich. State Med. Soc., April, 1921.

have had them for years. A disastrous feature of malignancy is always cachexia. Very few patients survive when it is well-marked. The interval of time between treatments depends upon the patient's tolerance of the rays and upon the appearance of the tissues. One tries to give the tumor the limit that the patient will stand in a given time, but this amount varies with each patient.

Surgery and radium and Roentgen-ray treatments must go hand in hand. They are not antagonistic but complementary. The one complication to be dreaded either following surgery or directly responsible to the radiation is infection. It may have been quiescent. But all rays, be they ultra-violet, radium or x -ray, have the tendency to bring an infection to a head. Pain in malignancy has nearly always proved an ominous sign. If the pain does not disappear under treatment, the prognosis is generally bad. If the pain increases after each treatment, radiation has to be abandoned. If initial pain disappears in the first weeks of treatment, the patients generally recover. Hemorrhage from any source endangers the life of the patient, and the rays quite commonly control the hemorrhage. In the normal individual the toleration of the organs of the body varies. The liver is the one organ that does not tolerate the rays at all, and the small bowel can stand only a certain limited amount. Therefore, when toxic symptoms like vomiting, profuse perspiration or weakness appear, we must give these parts time to recuperate. Organs containing large blood supplies, like goiters, lungs, and spleen, can easily be over-exposed, causing leukopenia, dyspnea and general toxemia. The blood and urine should be under constant control where heavy dosage is applied. The author believes that the rays actually produce something in the body of the patient that protects him and raises his immunity against a recurrence.

Action of Radium and Roentgen Rays on Lymphoid Tissue. Isaac Levin³ emphasizes the fact that the lymphocytes circulating in the blood are most readily influenced by radium and Roentgen rays, while all other normal types of leukocytes and the erythrocytes possess a greater resistance. The destruction of the polymorpho-

(3) Jour. Amer. Med. Ass'n., Sept. 7, 1921.

nuclear leukocytes is caused by the action of a lethal dose of the rays which produces a severe lethal leukopenia. The specific radiosensibility of lymphocytes explains the action of radium and Roentgen rays on normal and diseased lymphoid tissue, even when lymphoid organs are not directly rayed. This destruction of the lymphocytes within the lymphoid tissue is accompanied by endarteritic obliteration of blood-vessels and formation of dense connective tissue. Normal lymphoid tissue is comparatively less radiosensitive than the various types of hyperplasias of lymphoid tissue. Furthermore, simple inflammatory hyperplasias are less radiosensitive than the neoplastic hyperplasias. It is comparatively difficult to influence with radium and Roentgen rays bacillary infectious lymphomas like the tuberculous glands. Hodgkin's disease presents a type of actively proliferating neoplastic hyperplasia of the lymphoid tissue that is extremely radiosensitive. The opinion prevails that the action of the rays is only palliative and that ultimately the patients fail to respond to treatment. These unsatisfactory results are probably due to the fact that the treatment is attempted only late in the course of the disease and is not pursued with sufficient energy. In several cases the disease has been arrested for from six to eight years. Enlarged spleens shrink to normal size under the influence of radium or Roentgen rays. Lymphosarcoma is influenced by irradiation more promptly and completely than any other type of lymphoid hyperplasia. The ultimate results in lymphatic leukemia are worse than either in Hodgkin's disease or in lymphosarcoma. As myelocytes in conditions other than myeloid leukemia are also not radiosensitive, the myelocytes of myeloid leukemia which are not so readily destroyed by radium and the Roentgen rays must represent biologically a different type of cell more akin to a cancer cell.

Status thymicolymphaticus, a disease of childhood which consists of general lymphoid hyperplasia with enlargement of the thymus, which causes frequent attacks of so-called thymic asthma and sometimes sudden death, can apparently be cured by radium and Roentgen rays. Levin cites a case in point.

The Limitation of Radiotherapy of Malignant Tumors. Robert B. Greenough⁴ does not agree with the idea of highly exceptional susceptibility of cells to radiation. He points out that experiments have shown that radiation may produce four different results (1) living tissue may be destroyed *en masse*; (2) growth may be temporarily inhibited; (3) rapidity of growth may be stimulated, and (4) the manner of growth may be modified. In the practical application of radiotherapy to the treatment of tumors, the mass destructive effect of a lethal dose of radiation is necessary for the cure of malignant disease. In no case of actual cancer, has he succeeded in this purpose without the production of a destructive lesion. In many cases there is failure to destroy the disease entirely, and at some subsequent time the disease recurs. The cure of cancer (estimated in surgical terms on a three or five years basis) is not accomplished without massive and total destruction of the tumor by direct application of the source of radioactivity. The phenomenon of temporary inhibition of growth is often observed. Without gross changes in the appearance of the tissue, cells exposed to radiation may remain quiescent for a considerable period of time, only to wake to active and continued growth after this radium effect has passed away. In the clinic this phenomenon appears as the recurrence of a tumor apparently destroyed by radiotherapy.

Certain tumors of lymph-adenoid tissue, such as malignant lymphoma (Hodgkin's disease) and lymphosarcoma appear to exhibit a definite and positive sensitiveness to radiation in that, when they are for the first time subjected to deep radiation, profound changes in their structure take place—the tumor masses shrink and occasionally disappear, without undue damage to the normal tissues overlying the diseased. However, these changes are temporary rather than permanent, and although a recurrence of the tumor masses in the same or in other lymph nodes may again react favorably to radiation, sooner or later the sensitiveness is lost, and the patient ultimately succumbs to the disease. In myeloid leukemia, also, profound changes in the blood picture, in

(4) Boston Med. and Surg. Jour., June 16, 1921.

the size of the spleen, and in the patient's comfort result from deep radiation of the spleen; but, again, the improvement is temporary and is followed by recurrence of symptoms and ultimately death. In almost every fatal case of carcinoma of squamous-celled or glandular origin extension of the disease to the regional lymph nodes ultimately takes place. Radium treatments have been given in a very large number of these cases, but in no case has Greenough succeeded in destroying, permanently, the disease. Shrinkage in size of an enlarged node is occasionally observed; but, when this occurs, it is probably due to reduction of the accompanying inflammatory process rather than to a destruction of cancer tissue.

Cells engaged in mitotic cell division are generally believed to be more sensitive to radiation than resting cells, and it is not unreasonable to suppose that a part, if not the greatest part, of the supposed sensitiveness of cancer tissue to radiation is dependent upon the number of cells actually undergoing mitosis during the period of exposure. If this is so, a fractional destruction of the tumor only can be expected as a result of repeated deep radiation, for during each exposure only those cells in mitosis should be affected, and a diminishing but constant residue of unaffected cells would always remain to wake into activity and grow at some subsequent time, and produce recurrence. We must also recognize that repeated exposures to radiation produce a gradual loss of sensitiveness on the part of the tissues exposed, so that the attempt to accomplish a fractional destruction of tumor tissue by deep radiation is by this fact also made more difficult. The clinical observations of the results of deep radiation on cancer tissue are in accord with this theory; for, although inhibition or retardation of growth may be observed, the destruction of the tumor and the cure of the disease are not accomplished.

The ability of radiation to modify the growth of cells is shown in the application of radiotherapy to the relief of benign lesions of the skin, such as papillomas and keratoses. In these cases the destructive effects of radiation are not needed or desired. After a mild reaction the deeper cells of the epidermis, which have previously

been growing in an abnormal manner, begin to grow in a more normal manner; the abnormal cells are cast off and the lesion is cured without a scar. This action, while of the greatest value in the treatment of non-malignant lesions, can be counted upon but little in the attempt to eradicate malignant disease. No modification of growth of cancer cells short of death and destruction of every cell is sufficient to cure the patient of *cancer*.

Radiotherapy of Uterine Fibroids. F. J. Taussig,⁷ believes that radiotherapy is destined more and more to displace operation as patients learn to come early, before contraindications to its use have arisen. The dread of the knife has in the past kept many patients from consulting a physician, or, after they have consulted him, it has made them put off treatment month after month. If it is true concerning cancer that "in early recognition and treatment lies *hope* of cure," it is well to emphasize to our patients that in the case of fibroids "in the early recognition and treatment lies the *ease* of cure." As to the expectancy of cure after radium or Roentgen-ray treatment the author collects from literature 1,099 cases of fibroids with a percentage of symptomatic cure of 95.5 per cent., assuredly a sufficient justification for the more extensive adoption of this form of treatment.

Taussig enumerates the contraindications to radiotherapy, as follows:

1. *Size:* When the mass of the fibroid uterus is more than 12 cm. in its average diameter, operation is usually to be preferred.

2. *Location:* Submucous fibroids protruding through the cervix, subserous fibroids of considerable size with a definite pedicle, cervical fibroids and intraligamentous fibroids had better be operated on.

3. *Degeneration:* Rapidly growing tumors, calcified fibroids, necrotic fibroids, and those complicated with malignancy are not suitable for radiation.

4. *Age:* There is no absolute contraindication to radiation on account of age except so far as the desire for children or a preservation of menstruation makes myo-

(7) Jour. Amer. Med. Ass'n., July 30, 1921.

mectomy or subtotal removal of the body of the uterus preferable.

5. *Complications:* Pyosalpinx and ovarian cysts, except small retention cysts, are a positive contraindication.

The author shares with others a decided preference for the intra-uterine application of radium in fibroid uterus. Radium may cause leukorrhœa for a period of time; but it does not produce the pronounced intestinal derangements (vomiting, cramping, catarrhal stools) that so often follow Roentgen-ray treatment. The diagnostic curettement which should always attend a radiation for fibroid makes the intra-uterine application of radium a simple therapeutic measure.

Radiotherapy in Uterine Cancer. A symposium on this subject, participated in by R. Duncan, H. Schmitz, J. G. Clark and F. E. Keene⁸ reveals that substantial progress is being made by improvements in technique. Imposing statistics with remarkably favorable results, considering the malignancy of the disease, are being offered. The authors agree that uterine cancer when given early and appropriate radiotherapy is curable in a large percentage of cases. Curative treatment depends on early diagnosis, proper dosage, and technique. In recurrent and inoperable carcinoma, appropriate radiotherapy surpasses any other known therapeutic agent. Pain, hemorrhage and odorous discharges are relieved and there frequently occurs prompt improvement in the general condition of the patient. Life is prolonged, and there results a comparatively high percentage of clinical cures.

A combination of radiotherapy with surgery is not advisable. To apply radiation properly, it is necessary to employ such an intensity of radiation that the periphery of the bony pelvis is struck with the same intensity as the region in the axis of the pelvis, that is, the cervix. Otherwise, the peripheral cancer cells are stimulated to increased proliferation. Such a radiation treatment always causes a decided radiation sickness. During this period the patient could not safely be subjected to the additional trauma and shock of a capital surgical pro-

(8) Jour. Amer. Med. Ass'n., Aug. 20, 1921.

cedure. The operation must be postponed for from three to six weeks, during which time the patient will have recovered from the radiation toxemia. If the operation is performed within a few days after radiation, the patients succumb to sepsis and shock with alarming frequency. Should the operation be postponed to a later period, danger is still present on account of necrosis of tissue in the cervical canal which can not be avoided. These factors and the intense connective tissue formation in the parametrium, which renders hemostasis difficult, do not let it appear advisable to resort to pre-operative radiation.

Postoperative radiation is likewise discouraged. If during an operation, it is found that the cancer has invaded adjacent structures, or the probabilities are that cancer tissue has been left behind; then a combined radiation treatment must be given. It must be as intensive as if the panhysterectomy had never been performed, regardless of the consequences to the patient. As a matter of fact, patients of the borderline and inoperable groups, treated with a combination of radiation and surgery, usually quickly succumb either to sepsis or to a recurrence in spite of the most carefully executed radiation treatment. Or, while an irradiation subsequent to a hysterectomy may save the day, it may leave in its train a distressing and possibly hopeless fistula. When the uterus remains as a broad wedge of tissue keeping the bladder and rectum well apart and the domelike vault of the vagina preserved, with the carcinoma held centrally between the broad ligaments, the opportunity for successful work by the radiologist is greatly enhanced. When a hysterectomy has been performed, the elastic tissues may retract to the iliac walls and thus remove the cancer outside the zone of safe irradiation.

A combination treatment of gamma and Roentgen rays assures better results than the application of either agent alone. The radium must be inserted into the cervical canal, while the Roentgen rays are applied through the suprapubic and sacral regions. For the technique the reader must be referred to the original articles.

Injurious Combined Effect of Roentgen or Radium Rays and Topical Remedies. G. M. MacKee and G. C.

Andrews⁹ call attention to the fact that small doses of Roentgen rays or radium, combined with topical irritants in strength, may result in severe injury. Large, but perfectly safe, doses of Roentgen rays or radium, combined with mild topical irritants, may give the same result. Intensive and reactive irradiation, associated with topical irritants in strength, is the combination most likely to effect injurious results.

Hypersensitiveness is very marked immediately subsequent to a single intensive dose of Roentgen rays or radium. The return to normal is probably in accord with biologic laws; and, in the absence of visible reaction (erythema) or of permanent injury, the skin will react normally to topical remedies in one month. If there has been a first degree radiodermatitis, manifested by erythema, but no permanent injury, the skin is likely to remain hypersensitive for one, two or three months after the treatment. If there is permanent injury as evidenced by telangiectasia, atrophy or scarring, the skin may remain hypersensitive for months and even years.

Any drug, chemical remedy, or agent that is capable of effecting an inflammatory reaction in the skin may make the latter more susceptible to irradiation. Chrysarobin, scarlet R, medicinal iodine, mercury, pyrogallie acid, cantharides, resorcin, betanaphthol, tar, iodoform, sulphur, salicylic acid and other remedies of this type produce hypersensitiveness of the skin. They cause the least trouble when used as powders; they are more potent in solution; they are most potent in the form of ointments.

Precautions Against Damage to Radiotherapist. C. Regaud¹ presented the following practical conclusions:

The accidental absorption, by inhalation, of radium emanations is not dangerous except in a confined space. The rays of radio-active substances present dangers similar to those connected with Roentgen rays. Operators and attendants can protect themselves by forming the habit of: (1) taking judicious advantage of the law of distance (especially through the use of special tongs in performing manipulations), and (2) interposing be-

(9) Jour. Amer. Med. Ass'n., Nov. 5, 1921.

(1) Paris Letter, Jour. Amer. Med. Ass'n., July 23, 1921.

tween the operator's body and any source of radiation leaden screens several centimeters thick and impervious to penetrating rays.

Time is an important factor. No nurse should remain longer than two months in a radium service.

Elaborate rules in connection with this important topic are presented in a "Preliminary Report" by the "X-Ray and Radium Protection Committee"² from whose honorary secretaries (Dr. Stanley Melville and Professor S. Russ) copies may be had on application, care of Royal Society of Medicine, 1, Wimpole Street, W. 1, London, England.

Use of Blood Counts to Indicate the Efficiency of Roentgen-Ray and Radium Protection. J. C. Mottram³ suggests that effects upon the blood may serve as a guide in deciding whether or no the worker is being subject to over-exposure; or, alternatively, whether or no the devices designed for his protection are sufficient.

Even a single blood examination may give a warning of danger, if the count be near the low limit for normals. A considerable fall with a sustained low level in the repeated blood examinations of a single individual indicates that insufficient protection is being provided. If several workers in the same department present very low counts, this also shows that further protective precautions are required. In workers using soft Roentgen radiation special attention should be paid to the lymphocytes, because these cells are more likely to be affected than are the polynuclears or red cells.

ROENTGENOTHERAPY

New Roentgenotherapy in Cancer. M. J. Sittenfield⁴ describes advances made in Germany during the last year and a half. The technique has undergone great changes; in particular, accurate measurements have been established, thus making possible exact dosage in carcinoma, sarcoma and benign tumors. These improvements are obviously due to the construction of more powerful Roentgen-ray apparatus, and with it new tubes

(2) *Lancet*, June 25, 1921, and *Brit. Med. Jour.*, June 25, 1921.

(3) *Brit. Med. Jour.*, Aug. 20, 1921.

(4) *Jour. Amer. Med. Ass'n.*, Jan. 8, 1921.

to accept a high tension voltage. While with the older machines it was impossible to obtain sufficient radiation to penetrate further than from 3 to 5 cm. to an appreciable extent, the new type of inductor or transformer develops hard rays capable of penetrating the entire body. Formerly, the greatest intensity obtainable ranged from 80,000 to 140,000 volts, whereas the modern Roentgen machine operates with an intensity of from 180,000 to 220,000 volts. It was found that the bundle of rays emitted from a Roentgen-ray target at a certain point of filtration effects an even and homogeneous radiation, that can not be altered qualitatively by further filtration. This point is called the homogeneous point. These are the rays now used in the technique of modern roentgenotherapy.

The determination of the exact dosage was made possible by means of delicate instruments of precision, as the electroscope of Wulf, and the ionizing chamber of the new iontoquantimeter of Szillard. We are now able to give a cancer of the uterus, for instance, situated from 7 to 10 cm. under the surface, 40 per cent. of a lethal dose directed from the abdomen. Another 40 per cent. can be administered from the back and, if necessary, from 10 to 15 per cent. from each side, making a total of 100 to 110 per cent. of a skin erythema dose. As it has been established that from 85 to 90 per cent. of a skin erythema dose will destroy cancer tissue, it is easily possible to administer a sufficient and effective amount with this technique. If, however, the full cancer dose has not reached the center of the tumor mass, then the desired dose can be realized by placing a small amount of radium in the uterus. The important feature to keep in mind is that it is absolutely necessary that every part of a cancer of the uterus, for instance, receive a full and lethal dose to bring about the desired result. On the other hand, if any part of the tumor has not received the full dose, a recurrence is sure to follow. If the total amount absorbed by the tumor is 40 per cent. of a skin erythema dose or less, it will stimulate the tumor growth instead of destroying it. All parts of the tumor must receive the same homogeneous radiation, and preferably in one treatment, which may require six hours. Another

factor of great moment is the preservation of the connective tissue which is so essential in the recession of a tumor. Along with this it is important to conserve the adjacent normal tissue, and not to subject the bladder, rectum and colon to irreparable damage. Fortunately, the bladder and rectum tolerate a dose a trifle higher than the skin; and since the dose for carcinoma is 85 and that for the skin 100, the correct radiation dose allows enough free play to prevent damage to the bladder and rectum.

With the modern technique the results are so favorable that in Freiburg no cancer of the uterus has been operated on since Jan. 1, 1919.

Carcinoma of the breast does not adapt itself to the same method of radiation as that of the uterus, for in the breast the malignant growth is situated only from 3 to 5 cm. beneath the surface. The tube is put at a distance of from 70 to 90 cm. from the skin; thus, only the hardest and most penetrating rays are used through a filter of 0.8 mm. of copper. By increasing the focal distance, the time of obtaining an erythema dose is also greatly increased so that nearly nine hours may be required. If the patient is restless, morphine or scopolamine is ordered. Whenever there is axillary glandular involvement roentgenotherapy is preferred to the knife.

Throughout virtually all Europe it is the rule to administer a preoperative Roentgen-ray dose to the operative field, for it has been shown experimentally that radiated cancer cells do not grow on transplantation.

Carcinoma of the prostate is treated like a carcinoma of the uterus, with the addition of radium applied by rectum.

The sarcoma dose as a rule is smaller than that of carcinoma, namely, from 60 to 70 per cent. that of a skin erythema dose. Cases of osteosarcoma, osteomyelitis sinuses and fistulas, and tuberculous joints are treated with gratifying results. In uterine myomas the entire treatment is effected in one session of from one and one-half to two hours. During the treatment exact measurements are read from the iontoquantimeter in the vagina. The biologic dose for atrophy of the ovary is from 25 to 30 per cent. of a skin erythema dose. As much as 85 per cent. of all fibroids either shrink or dis-

appear entirely, and in virtually all cases castration results. Moreover, malignant degeneration of fibroids offers no contraindication to radiation, since radiation here is just as applicable as to any other cancer of the uterus.

Roentgenotherapy of Hypertrophied Tonsils. J. B. Murphy, W. D. Witherbee, S. L. Craig, R. G. Hussey and E. Sturm⁵ suggest the possibility of utilizing the well-known fact that lymphoid tissue is easily destroyed by the Roentgen ray for clearing the throat of excess of this tissue. In the series reported, only one patient received more than one treatment. With the mildness of the Roentgen-ray treatment recommended, there is no reason why it should not be repeated as often as desired, with the proper interval between exposures. Of thirty-six cases, showing the hemolytic staphylococcus and hemolytic streptococcus, thirty patients became free from these organisms by the fourth week after treatment. The disappearance of the hemolytic organisms of the throat, is not attributable to the direct action of the Roentgen rays on these organisms; but rather to the proper drainage of the crypts as the tonsil tissue atrophies.

Good results are also reported by W. D. Witherbee⁶ in about sixty cases with only two exposures and a maximum dose of $1\frac{3}{4}$ skin units of filtered rays for from three to seven minutes, according to the age of the patient.

Roentgenotherapy of Prostatic Hypertrophy. S. Stern⁷ found Roentgen-ray treatment of value in hypertrophy of the prostate. He believes that, by means of it, some patients may be saved an operation. However, patients advanced to catheter life can only be temporarily benefited by the treatment.

CURIETHERAPY

The Economics of Radium Therapy. Albert Soiland⁹ believes that, in view of the large investment required for carrying on adequate radium treatment, it appears

(5) Jour. Amer. Med. Ass'n., Jan. 22, 1921.

(6) New York State Jour. of Med., January, 1921.

(7) Amer. Jour. Roentgenology, June, 1921.

(9) Med. Review of Reviews, February, 1921.

rational that there should be established a stabilized fee table, sufficiently comprehensive to meet the exigencies of practically all radium work. Such a fee bill, in the hands of radiologists in general, would be of inestimable value in acting as a guide toward uniformity of professional radium charges. This would do much good, particularly in the case of migratory patients, who have radium treatment in different cities, the charges for which often vary to a degree bordering on absurdity. For the purpose of presenting tangible figures for discussion he suggests that, when circumstances permit, a lump sum be charged for the case. In localized or superficial conditions, where a few well-directed applications serve to eradicate the lesion, the charge is varied from \$50 to \$200. When, in such case, one is pinned down for a price for a treatment, it is given as from \$10 to \$25 per radium hour, not milligram hour; that is, radium, irrespective of amount, for one hour's application. In all non-malignant conditions of the female pelvis, where relief can be expected in from three to five applications, a flat fee of \$250 is entered. If compelled to state work at so much a treatment in this class of service, or when more prolonged treatment is necessary, as in malignancies, a charge of \$1 per milligram of element employed is made, irrespective of time. Thus \$25 for twenty-five milligrams, \$50 for fifty milligrams, would be charged. This usually covers the hospital cases, where the time of radium contact varies from twelve to twenty-four hours. In bladder, prostatic, and rectal cases, a similar schedule is adhered to, which also serves well in eye, mouth, and throat conditions.

“In all this work, of course, the great human element of kindly and wholehearted charity must not be lost sight of. It is the duty of every one of us to treat, to the limit of our capacity, all those who seek our help, whether or not they possess sufficient worldly goods for adequate remuneration.”

Radium Emanation. As physicians in general are not familiar with emanation curietherapy, (the therapeutic use of radium emanation), it might be desirable at this point to refer briefly to some of the most salient facts in connection with this heavy gas which is spon-

taneously and continually given off by radium. The change of radium into this gas occurs independently of the physical state or chemical combination of the radium and at such rate that in 1,780 years one-half of any quantity will have become transformed.

The distinguishing feature of the gas is that it is endowed with radio-activity, due to emission chiefly of rays analogous to the Roentgen rays. Inasmuch as the action of radium is due to the giving off of this very gas, which in turn produces radiant energy in its disintegration, the use of radium emanation is equivalent to the use of radium. The radio-activity of the gas is due to its breaking up to the ultimate form of helium, which occurs at such a rate that one-half of the radio-activity is lost in about four days.

Like other gases, radium emanation is slightly soluble in water, from which it is readily diffused into the air when the bottle containing such solution is left open. Shaking the water hastens the loss of radium emanation into the air. From 10 to 30 per cent. of the emanation in solution of water may be lost by pouring it from one vessel to another. Boiling such solution drives off the gas completely. Water may be charged with radium emanation by dissolving the gas given off from a solution of soluble radium salt such as chloride or bromide, or else by submerging the insoluble sulphate in a state of minute subdivision into the water to be charged. The latter is the simpler and more economic process. Radium sulphate contained in porcelain cylinders or porous clay plates is employed in such preparations as "Radio-Rem" or the "Sauberman Radium Emanation Activator." Such plates or cylinders can be employed repeatedly and their use continued indefinitely, as after about 1,800 years they will still have half of their radium content.

The amount of radium emanation may be estimated with a high degree of accuracy by measurement of the rate of discharge of an electroscope owing to ionization of the air under the influence of the emanation. Of the several units employed for this purpose the one that deserves universal adoption is the *curie*, which designates the quantity of emanation present when 1 gm. of

radium element is in equilibrium with its emanation. For practical purposes, this is too large a unit. The *millicurie* or 1/1000 *curie* is perhaps the most useful subdivision of this unit. Thus, the daily administration of 250 c.c. of radium emanation solution containing 1.5 *millicuries* to the liter, may be required to obtain results in arthritic cases. The *microcurie* which is 1/1000 *millicurie* is also sometimes employed in measurements. The Maché unit is less definite and too small for general use. Approximately 2,700 Maché units are equivalent to one *microcurie* of radium emanation.

Isidor F. Shapiro¹ suggests, for the purpose of stimulating the healing of inflammation, the use of eosine in 1 per cent. concentration (alcohol must be added to about 10 per cent. in order to dissolve the eosine in water), together with the radium emanation, the amount of which required to induce luminescence is almost infinitesimal, and therefore not capable of doing harm (only a few *millicuries*). It might be desirable to add 1 per cent. of fluorescein to the eosine solution. In view of the case reports of the remarkable success of a 1. per cent. eosine solution when exposed to light rays, the author thinks this suggested combination of exciting the eosin in deep locations by means of radium emanation, should find a wide field of application.

Radium Emanation in Large Dosage in Treatment of Chronic Joint Diseases. Paul Werner² reports a series of sixty cases of several varieties of chronic joint trouble with complete recovery in 6.7 per cent. and marked improvement in 48 per cent., that is, success in the treatment of at least 55 per cent. of the cases, and slight improvement or no result in 45 per cent. of the cases. This, in view of the therapeutically unsatisfactory nature of these cases, must be looked upon as a good showing.

Werner employed water made radio-active to as high a degree as possible and in the largest possible dosage. Starting with 1,000 Maché units daily the dose was gradually increased to 150,000 to 300,000 and in some cases 1,000,000 Maché units. Patients received their

(1) New York Med. Jour., March 16, 1921.

(2) Therap. Halbmonatsh., March 15, 1921.

PLATE IV.



Case I, aged 8½, on ski.—Rollier, page 226.

PLATE V.



A B C

Case 1.—(A) Child, age $4\frac{1}{2}$, arrived with 34 tuberculous foci, osteitis, perioostitis, adenitis, multiple fistulae, tuberculosis of both feet, right hand, peritonitis, and advanced tuberculosis of left lung. General condition very poor, advanced cachexia, high temperature, and albuminuria. (B) One year later—all tuberculous foci cured and fistulae closed. General condition completely transformed. (C) At age of $14\frac{1}{2}$; cure completely maintained in spite of the patient having lived throughout the war in Germany, where he underwent considerable privation.—Roller, page 226.



A



B



C

(A) Child with 17 tuberculous foci on arrival. osteitis, perlostitis, adenitis. One lesion in temporal region had been cured. Secondary infection, fistulae; affection of tracheobronchial glands and infiltration of right apex. (B) Complete cure six months later. (C) 13 1/2 years after establishment of cure. Wheelwright and agricultural laborer. Did more than a year of military training without a day's illness.—Rollier, page 226.

PLATE VII.



A



B



C

(A) Case of tenosynovitis and tuberculous arthritis of wrist, recurring after operation. Secondary infection, fistulae; renal tuberculosis, nephrectomy, tuberculous peritonitis; tuberculosis of right apex, small lupus on right cheek. General condition poor; habitus phthisicus. (B) The same patient one year later. (C) The same patient thirteen years after establishment of cure. In good health and very active as a nurse.—Rollier, page 226.

dose in small glass tubes of about 20 c.c. capacity, and were advised to drink this in small quantities during the day, and to fill the bottle each time with ordinary water and stopper securely so as to avoid as much as possible loss of radium emanation into the air of the bottle. The course of treatment lasted five weeks; and it has been found advantageous to repeat such courses at intervals. Only a few patients showed, after the use of large doses, unfavorable reactions, such as headache, dizziness, and insomnia. The best results were obtained in primary chronic polyarthritis. In arthritis deformans, on the other hand, while subjective improvement was obtained from it, no change in the objective findings was noted.

The author ascribes the favorable results to the affinity of radium emanation for lipoid tissue, such as the nervous system, which renders it eminently analgesic and antagonistic to inflammation. The latter action might possibly be assisted by the leukopenia produced by large doses. After the emanation has exerted its pain-relieving effect, active mobilization of the stiff joint may be undertaken.

"*Restitutio ad integrum*" can hardly be expected in advanced chronic joint disease by this or any other method, but Werner believes that we have in radium emanation, when used in sufficiently high dosage, a remedy which either alone, or in combination with other treatment, often yields results not obtained in any other way.

Radium Emanation in the Treatment of Goiter. Wallace I. Terry³ suggests in the treatment of the bad risk cases of exophthalmic goiter to introduce radium emanation into the substance of the thyroid. Under local anesthesia, a spinal puncture needle of small caliber is introduced into the thyroid with an emanation tube, representing 6 or 7 millicuries loaded in the hollow needle. The tube is pushed out of the needle by an obturator slightly longer than the hollow needle. This procedure is repeated until all the tubes containing radium are deposited in various parts of the thyroid gland. The emanation thus acts from within the goiter and tends

to inactivate it and prepare the patient for operative treatment should it be deemed advisable.

It is not expected that this form of radium treatment will supplant ligations, but it may sufficiently improve the patient after the lapse of from four to ten weeks, for partial lobectomies.

PHOTOTHERAPY

Phototherapy in Rachitis. P. Erlacher⁴ obtained definite improvement and, in most cases, cure, as evidenced by monthly comparative roentgenograms in forty-six patients with rickets, by means of quartz lamp therapy. The treatments are given daily, at first five minutes' treatment each to the abdomen and back at one sitting; the time was increased later by two minutes at each sitting until fifteen minutes each was reached. It required usually from forty to sixty sittings. Correction of deformities should be taken care of before irradiation.

HEAT

Heat Rays in Ear Disease. W. Oekin⁶ finds heat rays of great value in many varieties of ear disease. While discarding the use of the quartz lamp as of little help, he employs the "Sollux Lamp," a 600 candle-power nitrogen bulb with a tungsten filament yielding a powerful white light which produces a great deal of heat, the rays of which are concentrated by means of suitable reflectors. He administers the treatment at a distance of 10 cm. from the ear for the duration of one hour, at an average, using a protective eye glass without steel parts as these are liable to become hot and cause burning of the skin. In a large number of treatments no damage whatever has been produced. The author knows of no contraindications to this treatment.

The effect of such treatment is a marked hyperemia which extends into the depth and continues for quite a time. Oekin knows of no other measures that will pro-

(4) *Wien. klin. Wochenschr.*, May 19, 1921.

(6) *Therap. Halbmonatsh.*, Dec. 1, 1920.

duce a hyperemia of such degree. In a series of fifty cases of acute otitis media, he has succeeded by employing this treatment twice daily to relieve pain at once, to avoid the necessity of incision of the drum head, and to reduce the average duration of the disease by at least one-third. In acute otitis media with perforation of the drum head an average of ten treatments administered once a day (minimum of three and maximum of twenty) succeeded in producing complete cure of discharge, the pains being relieved with the first treatment.

Even in five cases of perforation occurring in otitis media with beginning mastoiditis, such treatment twice daily succeeded in rendering other therapy unnecessary. In two cases of mastoiditis in which operation was required, the heat ray treatment proved itself a grateful postoperative procedure.

A marked result was obtained in a case of otohematoma which disappeared after ten irradiations.

In 100 cases of furunculosis of the external meatus, the pain was relieved after the first treatment and in one-third of the cases no suppuration occurred, in others discharge of pus occurred without the necessity of incision and from two to six treatments were sufficient to effect a cure.

In all these conditions, the treatment relieves pain, increases absorption thus hastening healing and preventing suppuration in early cases thus lessening the necessity of frequency for operative interference.

[Prolonged very hot irrigation of the ear is also very effective in relieving earache; and, as no other apparatus than a fountain syringe is required, it is much more generally applicable so long as there is no perforation of the drum head.—ED.]

Local Hot Sand Baths. While general hot sand baths for adults are too troublesome to be of much practical value, partial hot sand baths have advantages over hot air baths and mud baths in certain gynecologic cases as shown by R. Aschenbach.⁷ A more intense heat (62° C.) is borne because of the readiness with which perspiration is absorbed by the sand and the heat remains practically constant for hours. Thus, a marked flow of

(7) Centralbl. f. Gynäk., June 25, 1921.

blood to the genital organs takes place, whereby rapid absorption of exudates is effected.

CLIMATOTHERAPY

Heliotherapy in the High Alps. A. Rollier⁸ believes that, up to the present, science has not yet invented an adequate substitute for sunlight; and that, while heliotherapy may be carried out in any place where the sun shines, the best results are obtained in high altitudes for the following reasons: To reach the sea-level the sun's rays have to pass through the whole thickness of the atmosphere. In addition to this, over all our big cities the air is rich in mists, dust, and microorganisms which absorb both heat and light-rays in a proportion sometimes as high as 95 per cent. This absorption not only deprives the patient of a large number of useful rays, but by heating the air may give the sun-bath a relaxing instead of a stimulating effect. At high altitudes, on the contrary, the air is transparent, free from solid particles, and easily traversed by the sun's rays, which pass through without absorption, and warm and invigorate the body of the patient while leaving the air cool and fresh. For this reason a much greater intensity of direct sunlight can be borne at high altitudes and heliotherapy may be practiced in every month of the year.

Rollier makes a plea for that much ill-used organ, the skin. Europeans, he says, are apt to regard with a complacent superiority the way in which less enlightened races maltreat their bodies (*e. g.*, the feet of Chinese women), but we ourselves would do well to imitate more closely certain less cultivated races with regard to the treatment of the skin. By covering the body with clothes every one of its functions is interfered with to a greater or lesser extent. He has frequently noticed that the resistance of a patient against disease is closely proportional to his degree of pigmentation, and pigmentation does not take place under clothes. It is a well-known fact that cutaneous sensation is much more delicate in the uncovered regions of the body; and it is equally obvious that clothes, by preventing free evapora-

(8) Lancet. March 19, 1921.

tion, interfere with the excretory functions of the skin. The contrast between the tolerance to wide ranges of temperature shown by the face and hands and the extreme sensitiveness of the rest of the body gives some idea of the extent to which disuse atrophy of the heat-regulating mechanism has taken place. The increased vascularity of the skin produced by the sun's rays causes considerable thickening of the organ itself, and also appears to result in an increase of the adipose tissue beneath the skin and improved muscular development. When these facts are borne in mind the frequently quite remarkable results obtained by heliotherapy are to a large extent explained, as it is only to be expected that the return of these numerous and important functions to the skin would have a most beneficial effect on general health.

The secret of the effect of sun's rays on pathologic processes is that, while highly toxic to microorganisms in general (and to the tubercle bacillus in particular), the solar radiations are not only harmless, but actually beneficial to the cells of higher animals. The specific action of sunlight was of great assistance in the treatment of suppurating war wounds. The sun appears to increase the rate of disintegration of cells damaged beyond repair, while stimulating the activity of the undamaged cells. A torpid lesion (such as varicose ulcer) demonstrates particularly well this citatrising action of the sun. Anemia and rickets, essentially diseases of deficient sunlight, are similarly amenable to heliotherapy.

It is, however, in tuberculosis and especially in the surgical varieties (bones, joints, glands, peritoneum, etc.), that the action of the sun is seen to its fullest extent. The prognosis of surgical tuberculosis is exceedingly favorable when the lesion is closed. This can hardly be said to be the case when secondary infection with pyogenic organisms—on which the sun has a much less specific action—has taken place. Experience with cases of this type has made Rollier more than ever insistent on the necessity of beginning active heliotherapeutic and altitude treatment as early as possible in all cases of surgical tuberculosis. He gives the following statistics for osteo-articular tuberculosis since 1914.

| | Children | Adults | Total |
|--------------------|-------------|---------------|---------------|
| Cured | 681 (86.5%) | 1,065 (77.2%) | 1,746 (80.5%) |
| Improved | 51 (6.5%) | 191 (13.8%) | 242 (11.2%) |
| Stationary | 43 (5.5%) | 104 (7.5%) | 147 (6.8%) |
| Worse and deceased | 12 (1.5%) | 20 (1.5%) | 32 (1.5%) |
| | 787 | 1,380 | 2,167 |

The cases that remained stationary, or in which the patients became worse, or died, nearly all suffered from secondary infection (Plates IV to VII).

Rollier describes his technique as follows:

"Exposure always begins with the feet; the legs, thighs, abdomen, and thorax follow in this order with an interval of a varying number of days between each. Only a few minutes' exposure is allowed to each part on the first day of insolation; this amount is gradually increased until at the end of a period of time, which varies with each subject—degree of pigmentation and absence of excessive reactions being the criterion—the patient is able to expose the whole body to the sun for several hours daily without any inconvenience either in summer or winter. Secondary infection without free drainage, pulmonary and abdominal tuberculosis, are conditions in which increased caution is necessary. Far from contra-indicating heliotherapy, however, they are greatly benefited by this form of treatment if properly carried out. Plaster apparatus is a great hindrance to heliotherapy and is almost invariably discarded, as not only does it interfere with the local action of the sun on the diseased part, but it also causes muscular atrophy, which is a great disadvantage when return of function begins, and compares most unfavorably with the thick covering of well-developed muscle which is usual with heliotherapy, and forms an admirable support for a weakened vertebral column or joint. These cumbersome devices of plaster should be replaced by simple arrangements of webbing straps which give complete immobilization and adequate extension while permitting free access of air and sun."

[For orthopedic technique used for each localization the disease, the reader desirous of further information is referred to the author's book, "*La Cure de Soleil.*"—Ed.]

As an adjunct to heliotherapy the work cure is a valuable factor. Even in serious cases of tuberculosis of the vertebral column, hip or knee, much benefit can be derived from such handicrafts as wood-carving, weaving, basket-making, metal work, painting on wood, toy-making, etc. Not only does this work cure benefit the patients mentally, but, by enabling them to continue earning their living during treatment, it has in many cases made it possible for patients, who would otherwise have left only partially cured owing to financial difficulties, to continue treatment until cure was complete.

For maintenance of cure it is obvious that for some years at least the patient should work in suitable surroundings. For children an open-air school where sun-cure can be continued is the ideal half-way house for the convalescent. For adults, agricultural work has an admirable effect in consolidating a cure.

Heliotherapy should also be employed in prophylaxis. We now know that surgical as well as pulmonary tuberculosis is in the great majority of cases secondary to infection of the tracheobronchial or mesenteric glands; this usually takes place in childhood and may remain latent for many years, only becoming active when, for some reason, the resistance of the body is lowered. For these delicate or predisposed children we should apply the same treatment as for convalescents. They should have as much fresh air as possible day and night, with plenty of good and simple food, of which fresh farm produce forms a large proportion. School work is reduced to a subsidiary position, its object being merely to keep the mind in discipline; the use of very light folding desks and stools makes it possible for lessons to be held in the fields and woods, the site being varied according to the heat of the day. In summer the children spend the whole day in bathing suit; and even in winter clothes can often be dispensed with, at all events during rest hours in the solarium. Much attention is given to Swedish drill. The results obtained give reason to believe that in almost every case the disease may be completely eradicated before any manifestations take place, thus avoiding much suffering and expense.

Therapeutic Value of Sea Coast Climate. C. Häberlin⁹ reports results of his twenty years' experience with ocean climate in many thousands of patients.

In bronchial catarrhs, especially in children who are extremely susceptible to taking cold, it is the constant observation that, in spite of less clothing and liberal exposure to the open air, they do not take fresh colds, or at most develop a coryza at first, which, however, does not go on to bronchitis as it would have at home. What is still more important is the fact that in a considerable proportion of cases (80 to 90 per cent. among over 5,000 children), colds and catarrhs did not reappear in the ensuing winter and spring; as the parents often said, "the children had changed entirely."

Among 100 patients with asthma, from forty to fifty had no attack at the sea coast and from thirty to forty were much relieved. However, complete cessation of attacks after leaving the sea-shore is a rarity, occurring in scarcely more than 10 per cent., though considerable improvement was noted in about 60 per cent., while 30 per cent. showed no permanent benefit.

Scrofulous children with dermatitis, eye, nose, ear and throat inflammations, showed improvement in more than one-half of the cases. Adenoid vegetations were not benefitted by sojourn at the sea-shore, and should be removed before the children are sent there. Lymphatic glands diminish in size and are cured by sufficiently prolonged stay at the sea shore in perhaps 80 per cent. of the cases, though the time required may be from one-fourth to a whole year. In the treatment of these cases direct use of sunshine is of undoubted advantage. In chronic bone and joint diseases, the sea-shore is properly considered the best climate and cures have been secured in approximately 70 per cent. of cases. France which has an uninterrupted thermic scale of coast climates has found that the channel coast is the most suitable for bone tuberculosis. The sea coast is also very beneficial in cases of rickets.

Regarding the manner in which these effects are brought about, Häberlin considers the increased metabolic activity (2,700 calories per square meter *versus*

(9) Ther. Halbmonatsh., Jan. 1, 1921.

1,445 in the city) responsible for increased appetite, gain in weight, and increased rate of growth. Retention of calcium and phosphorus has been demonstrated as well as of nitrogen. The latter is due to growth of muscle, which is also demonstrated by increase in the power of the right hand after six months' stay at the sea-shore. There is an increase in the hemoglobin by 10 per cent.; and, in cases of anemia, by 20 to 30 per cent. The red corpuscles increase by about one-half million.

The respiratory passages are favorably influenced by the purity and moisture of the atmosphere. In view of the fact that breathing of impure air causes a constriction of the bronchioles—a defensive mechanism—the breathing of sea air gives one the subjective feeling of greater ease in breathing, which is specially appreciated by the asthmatic. This action may be determined by measurements. Thus it was found that there was an average increase of 2 cm. in inspiratory excursion among 6,000 children. There is also a decrease in expiratory collapse of the chest by 0.3 cm. This improvement in respiration means improved nutrition for the lungs, as well as the benefits which improved pulmonary ventilation give to the circulation as well as the whole system.

The constant motion of the air at the sea coast is a stimulus to the skin causing an improved perfusion of the blood in this organ. This results in a diminution in the amount of blood in the internal organs, which means a wholesome redistribution of the blood in the sedentary town dweller with pale skin, cold hands, cold feet and congested internal organs. There is no doubt also that an important psychic influence is shown by improvement in the quality of mental work done by the children under investigation. Clinical results leave no doubt that there is an increase in the defensive mechanism of the system against infection. To obtain all these benefits it is of great importance that the patient stay at the sea-shore. A very short distance away from the shore there are such meteorologic differences as to jeopardize success. Not every patient is capable of exposing himself to the full action of the sea air without harm, hence expert advice is required for best results.

Preventive Medicine

EDITED BY

WM. A. EVANS, M.S., M.D., LL.D., D.P.H.

WITH THE COLLABORATION OF

G. KOEHLER, M.D.

PLATE VIII.



STEPHEN SMITH, M. D.

Dr. Stephen Smith, now 99 years old, is a striking landmark in the progress of knowledge of public health and personal hygiene.

Having been Health Commissioner of the Metropolitan Board of Health of New York City in 1865, and for several years thereafter a member of the U. S. Board of Health, appointed in 1879, and always active in public health work, he has witnessed the phenomenal improvement in public health of the last sixty years.

His long, healthy life and vigorous old age furnish the best proof of his knowledge and use of the rules of personal hygiene.

Photograph by courtesy of the American Journal of Public Health.

INTRODUCTION

During the latter half of 1920 and all of 1921, the general health of the people of the United States was good beyond any reasonable expectations in so far as we can judge by the death rate.

Never before in the history of vital statistics have the death rates been so low, particularly if we omit from 1920 those earlier months during which there were local recurrences of influenza. Such low death rates cannot continue for many years. Even were ideal health conditions to prevail such low death rates would shortly carry large groups of the population into age periods where the death rate is high and will continue to remain so for a long time.

The weekly bulletin of the Census office indicates that certain cities have death rates far below even the very low average referred to. This is due to large movement of population from such cities as the result of business conditions.

The decline in the death rate from consumption, much in evidence in 1920, has continued during 1921.

It is clear that the predictions of an increase of consumption in the wake of influenza have not come true. The relation between influenza and consumption is not understood, but it is significant that the latter disease has declined so steadily since 1918, a decline which can not be wholly explained on the theory that a large proportion of the consumptives died during the influenza epidemic and were buried under death certificates giving the pandemic disorder as the cause of death.

Doubtless this happened in many cases, but by no stretch of the imagination can it be said that this explains so widespread a sequence, and one which shows no tendency to let up now that we are in the fourth year elapsing since the great epidemic.

There has been a manifest, though slight, disposition toward an increase in typhoid fever in most sections during 1921 as compared with 1920. One suggestion is that the several million soldiers and army attachés are losing the immunity gained by vaccination during the war. This group makes up something like 5 per cent. of the total population. These individuals are in the midst of the age periods in which typhoid evidence is greatest, and it has been from three to six years since they were immunized by vaccination.

Figured on this basis, an increase of typhoid fever of less than 5 per cent. as compared with 1917, would still indicate an improvement in so far as other factors in typhoid etiology are concerned.

The volume of laboratory work done on influenza and coryzas during the year has been large.

The biologic characteristics of the influenza bacillus have been especially studied. We know far more about this organism than we did in 1918. The opinion seems to be crystallizing that, however much it has to do with ordinary coryzas, it was not the active cause of the influenza we had in the great epidemic of 1918. The principal factor in that pandemic was some still undiscovered organism, though much of the symptomatology and other clinical features of the disease as met with were due to streptococci, pneumococci, influenza bacilli, and other complicating organisms.

As I judge the trend, opinion is crystallizing on about that basis.

It is reasonable to hope that the research work done on the bacteriology of the upper air passages in carriers, convalescents and persons suffering from coryza, may eventually lead to methods of prevention and cure of coryzas, bronchitis, tonsillitis and pneumonia.

In the control of venereal disease the year has witnessed no new type of activities. The new dispensaries and hospitals have been opened and the work of educating the public has gone on. In the State of Pennsylvania and in Buffalo, New York, there has been some effort at medical prophylaxis, but governments, state and local, have been hesitant about attempting that part of the Army program.

In certain sections of the country the authorities are not satisfied with the diphtheria situation. The literature indicates a greatly broadened interest in the Schick test and in T-A vaccination.

As this is written, the American Public Health Association has just finished its fiftieth annual meeting.

The outstanding feature of this meeting was the reception given the man who, as health commissioner of New York City, called together the Cholera Conference, out of which grew the American Public Health Association. That man—Stephen Smith—is practically one hundred years old. At the banquet given in his honor, the other speakers indulged in introspective speeches, comparing the present with fifty years ago.

Stephen Smith made a forward-looking speech.

He called for a popular recognition of one hundred years as the proper span instead of the Psalmist's limit of seventy, with an occasional permit for eighty.

Dr. Stephen Smith emphasized the importance of personal hygiene.

Inferentially, he advised the thousand health officials present to add personal hygiene to the list of public health activities for which they hold themselves responsible.

W. A. EVANS.

PREVENTIVE MEDICINE

MEDICAL ECONOMICS

WORLD WAR AND DISEASE

Achievements of U. S. Army Medical Department in World War. M. W. Ireland¹ gives a review of the achievements of the U. S. Army Medical Department in the World War. The article must be read in its entirety to get a comprehensive review of the problems which the Medical Department had to confront, and the success that was obtained in carrying it from a stage of comparative unpreparedness to the grand scale such as prevailed at the time of the armistice.

In reference to preventive measures, Gen. Ireland states that in this war we first learned to go after the sources of disease instead of waiting for it, through a gradual realization of the fact that the individual, particularly the individual carrier, is more dangerous than the disease itself. The isolation of contacts and suspects, as well as of carriers, in such communicable diseases as measles, meningitis and influenza, although not a new feature in military or civil sanitation, was first carried out on a large scale in this war.

Public Health Problems in Europe. C. E. A. Winslow² reports that in the public health field, the menace of extensive post-war pestilence has so far been held in check. Typhus is still a grave problem in Poland and Russia, and the case-fatality rate this spring has been abnormally high. Nevertheless, it is believed that this disease is in general under control.

Mr. Knud Stouman estimates that in the eleven newly formed countries of central Europe the tuberculosis death rate for all ages ranges between 300 and 600 per

(1) Jour. Amer. Med. Ass'n., March 19, 1921.

(2) Nation's Health, June 15, 1921.

100,000, which corresponds to some 400,000 deaths a year.

The infant welfare work which was so stimulated during the war has brought down the infant mortality rate for England and Wales to eighty deaths under one year per 1,000 living births for 1920, as against eighty-nine for the previous year and 108 for 1913. Campaigns against tuberculosis and venereal disease are also being developed with remarkable effectiveness, and altogether England is probably leading the world in public health activities.

In France, there is unusually active interest in child welfare work.

The American Red Cross is operating a training school in Prague and two training schools in Poland which, with the school in Bucharest, and the projected school in Belgrade, are likely to exercise an incalculable influence on the development of public health nursing in central and eastern Europe.

Professional Lessons of World War Applied to Civil Life. Under this caption H. N. W. Gray⁵ outlines the public health and medical lessons that may be drawn from experiences in the recent world war. He urges that the citizen, the civilian worker, be regarded as a combatant fighting for the nation's welfare, and that this worker should be educated and kept fit for his warfare just as carefully as the soldier. In certain circumstances he may require equally intensive training.

The civilian must be kept in good health for his work in his particular fighting line, whether in the street, shop, or factory, and if disease or accident should overtake him, he must be made fit again to join his unit as soon as possible.

Under stress of war at the front, no post could be maintained for long unless good work was done. Here is our first lesson. Should not the same rule be applied to those in responsible positions, and especially in our schools of learning and in our hospitals?

One of the great developments in connection with the medical service of the war was that of "team work." The advantages of this were already demonstrated in

(5) Brit. Med. Jour., Jan. 22, 1921.

civil life, notably on a large scale in the Mayo clinic in America.

The most striking phenomenon of the war was the way in which the young man came to the front. As time passed, positions of great importance became filled with increasing frequency by young men.

SOCIAL MEDICINE

Future of Private Medical Practice. Frank Billings⁶ is of the opinion that the private practitioner does not occupy the same position that he formerly enjoyed. This, he attributes, in part, to the change in living conditions of the population, and especially to the advances made in modern medicine.

He considers that primarily the correction of conditions for the improvement of the status of the general practitioner implies the relation of the medical profession to the lay public. Billings is of the opinion that too often the medical profession is apt to consider itself as separate from the public. The fact is that it is only a small part of the general public. In round numbers there are about 150,000 licensed physicians in the United States, while the population approximates 110,000,000. If we are to consider anything which shall be of lasting benefit to the medical profession, it must afford the lay public equal consideration in relief from disease and injury. Therefore, in a consideration of the measures which must be instituted to improve the status of the private practitioner, we must keep in mind the welfare of the public.

As to general remedial measures, such as state medicine, health insurance, health centers and group medicine, he states that if the medical profession approves of the suggestions made for the establishment of health centers, we shall have a rational basis and argument for more complete organization of the profession. These centers will promote the public welfare, and at the same time will provide facilities for the diagnosis and treatment of patients by the medical profession, and

(6) Jour. Amer. Med. Ass'n., Feb. 5, 1921.

will stimulate postgraduate study and professional improvement.

Rural Health Centers. V. C. Vaughan⁷ states that there is at the present time ample justification for both the rural physician and his patient to demand for themselves better facilities for diagnosis and treatment. He is of the opinion that rural health centers, properly organized, will solve these problems. Such centers are to be established in local districts and, by majority vote of the citizens, shall have the right to establish hospitals, both general and contagious, including tuberculosis sanatoria. These hospitals are to be well-equipped with laboratories and other diagnostic facilities.

Every legally qualified physician in the community should have the right to utilize such hospital, its laboratories and its library. The community hospital should be a place where each physician in the community can find all the facilities necessary to keep himself in the front ranks of the profession. In fact, the community hospital would serve as a graduate school; specialists could be called to the laboratories and to the diagnostic rooms and give instruction on all recent advances. For instance, the application of the Schick test, and the inferences to be drawn from the reactions obtained, could be demonstrated.

Vaughan suggests that preventive and curative medicine should be combined in the community hospital.

Such a plan of medical organization; especially in rural communities, he thinks is the best possible way of placing all physicians on the same level so far as opportunity is concerned, and of giving to all citizens the benefit of scientific medicine, both preventive and curative.

Training of Home Nurses. The successful inauguration of a short course in home nursing given in Chicago in connection with the Department of Health is reported by J. D. Robertson.⁸ The school was opened in 1919 with a three-fold object in view: First, to provide for the expected recurrence of influenza; second, to train a body of women who would render nursing service at a

(7) Jour. Amer. Med. Ass'n., April 9, 1921.

(8) Amer. Jour. Pub. Health, February, 1921.

wage within the means of the average family; third, to popularize preventive medicine.

The course consists of lectures and demonstrations for a period of two months. Each class meets three times a week for two hours at a time. One hour of each period is devoted to lectures and the other hour to nursing demonstrations. There are both afternoon and evening classes, in order to enable the housewives of the city to select the time of day that is most convenient to them.

No fee is charged for the course, but a payment of five dollars is required to cover the cost of graduation, including a certificate and a syllabus of the course of lectures.

Many of the graduates do not wish to nurse outside of their own homes, but that makes no difference to a health officer. If a housewife can nurse her own sick, she makes no call upon the nursing supply of the community, and her sick are cared for.

The women who have attended the school average around 40 years of age; more than half of them are married or widowed. Life itself has taught them how to meet family and community problems. They need no special training in that matter. They need only a training in the fundamentals of nursing, and that, Robertson contends, they get readily in eight weeks.

[Up to November 1, 1921, 8,500 women have been graduated from the school.—Ed.]

PUBLIC HEALTH ADMINISTRATION

Useless and Useful Health Activities. L. W. Hutchcroft⁹ says that while some of the ordinary activities of state and local health departments are of unquestionable value in conserving the public health, others are relatively ineffective or actually harmful. It must be admitted that a part, and in some instances a considerable part of the energy of many excellent health departments is devoted to combating imaginary dangers or is applied to tasks that have only a remote bearing on the public health. This condition, as a rule, is not due to ignorance

(9) Wisconsin Med. Jour., February, 1921.

on the part of the health officials but to the pressure of public opinion.

It is surprising how many people still believe that the chief function of government in promoting health is to clean streets, remove garbage, abate nuisances, inspect grocery stores, meat markets, toilets and other work having to do primarily with cleanliness and other conditions which may interfere with the peace and comfort of the general public.

Our best sanitary authorities agree that improper garbage disposal has very little to do with the spread of disease in a sewered city, or that typhoid fever, diphtheria or other germ diseases are caused by sewer gas, tin cans, ashes, decaying vegetables or other waste. It often happens that with the beginning of a typhoid epidemic slovenly methods of handling harmless household refuse and the proper cleaning of streets and alleys are strongly emphasized and public attention is diverted from the real causes, such as the water supply, milk supply and contact infections.

The careful supervision of public water supplies is necessary to prevent typhoid fever. The milk supply must also be given careful attention to prevent scarlet fever, typhoid fever, tuberculosis and other milk-borne diseases.

Communicable disease carriers, such as typhoid carriers and diphtheria carriers, are now recognized as important agents in the spread of disease. The early detection, isolation and treatment of carriers must be provided for in proper disease control.

The examination of school children is also very valuable in disclosing physical defects interfering with the healthy development of the child and also in locating disease carriers and mild unreported cases.

In brief, the measures which Hutchcroft considers vital activities in any health organization are health education and the proper control of all germ diseases.

Minimum Organization Standards for Health Departments. Carroll Fox¹⁰ suggests that the appropriation necessary to maintain a minimum health organization varies from 50 cents to \$1.00 *per capita, per annum*. He

(10) Jour. Amer. Med. Ass'n., Sept. 18, 1920.

thinks that in a city of 10,000 population, 75 cents *per capita* would be sufficient to maintain the minimum organization. The health officer must perform the duties of bacteriologist, epidemiologist, school, milk and food inspector, etc.

In a city of 25,000 population, 75 cents would hardly cover the expense, as a city of that size should have a small isolation hospital. In this organization the epidemiologist performs the duties of a bacteriologist, and he divides the duties of school inspector and dispensary physician with the health officer.

It will be noted that no provision is made for the collection of garbage and other city wastes, street cleaning, etc. These activities can well be omitted in considering a health department, as they quite properly belong to a separate department of the city government.

Rôle of Sanitary Work in Health Administration. W. J. Cox¹ says that in the actual administration of sanitary work, one finds that the medical officer of health is very much dependent on the good offices of his sanitary inspector. The sanitary inspector should be eminently a practical man and one who is well endowed with tact and a pleasant personality, for his is a most difficult job.

Cox holds that bad housing and over-crowding are matters at all times deserving the attention of sanitary inspectors, for by these conditions the spread of infectious diseases is favored, and the inconvenience and discomfort of over-crowding produce a mentality which is favorable to the development of minor ailments.

Rôle of the Isolation Hospital. In a lengthy essay on this subject, A. K. Chalmers² bases his conclusions on the study of three diseases, *viz.*: scarlet fever, diphtheria and typhoid fever, in Scotland. He selects these three diseases because, while they have a fairly comparable isolation rate, their epidemiologic features are frankly different. One declines, another moves in wide fluctuations, a third definitely increases, despite a rapidly increasing rate of isolation common to all.

He tries to determine what features in the natural history of scarlet fever and diphtheria are not met by

(1) *Med. Officer*, Jan. 22, 1921.

(2) *Lancet*, Nov. 20, 1920.

isolation, and such other preventive measures as have coincided with the reduction of enteric fever.

In the first decade of notification, the enteric fever attack rate almost doubled itself, being 884 per million in 1892 and 1657 in 1898. This latter rate was repeated in 1901, after which it fell rapidly. For the last ten years the fall has been rapid and almost continuous, and in 1917 the attack rate was only 82.

The difference between the attack rates at the beginning and end of the period are sufficiently striking: In 1891-95 this rate averaged 1,129 per million; in 1915-19, 144. In 1891, 60 per cent. of the cases were removed to hospital; in 1895, 75 per cent. In 1915-19 it varied between 92 and 97 per cent. In 1910 and 1915 all the known deaths from the disease occurred in hospital. It is worthy of note, however, that despite the phenomenal decrease in prevalence the case mortality has remained not only high, but is fairly stable. In the earlier years it averaged 17, in the later, 18 per cent. Prevalence and morbidity are completely unrelated.

In scarlet fever, by way of contrast, the case mortality in hospital cases declined from 6 to 2 per cent., and in home cases is correspondingly low. Removals to hospital rose from 63 to 95 per cent., but the attack rate has markedly fluctuated with a tendency towards maxima at intervals of seven and ten years. The peaks of subsequent years are, however, lower than that of 1892. Compared with enteric fever, the attack rate is always on a high level.

Diphtheria, including membranous croup, differed in the character of its movement both from enteric and from scarlet fever. In the main it rose instead of falling like enteric, nor has it any of the short-time but wide fluctuations of scarlet fever. It is rather a movement of mass which takes about twelve years to complete. In Glasgow the isolation rate rose from 16 per cent. in 1891 to 57 per cent. in 1901; 90 per cent. in 1911; and an average of 93 per cent. in the years 1915-19. On the other hand, the fatality rate fell from an average of 26 per cent. in the years 1891-95, to 16 per cent. ten years later, and an average of 11 per cent. in the last five years.

From the figures presented, Chalmers concludes that it is not isolation that has failed, but that our limited knowledge of the causes of spread is as yet unable to supplement it by suitable action in other directions.

GENERAL SANITATION AND HYGIENE

ATMOSPHERIC CONDITIONS AND VENTILATION

Effect of High Wet Bulb Temperature. A. Breinl,⁵ in an inquiry into certain of the physiologic functions of wharf laborers in Townsville, proved that there is a general tendency for the rectal temperature to rise and remain at a higher level with higher wet bulb readings; it is, however, noteworthy that even when the wet bulb temperature reached 30° C., the averages for rectal temperatures were only between 37.7° and 38.3° C., with a maximum of 38.8° and a minimum of 37.5° C. The heat regulating mechanism of the laborer was not severely affected and he was still able to maintain a temperature equilibrium, although at a somewhat higher level.

The average pulse rate did not show constant variations, perhaps it was slightly higher on hot days.

The skin shirt temperature did not vary greatly, but was much lower in the men working in the freezing room.

The average systolic blood-pressure did not present constant changes, although it showed a tendency to fall with the progress of the day, concomitant with profuse sweating. The diastolic blood-pressure followed closely the course of the systolic pressure.

These observations carried out on a large scale showed that under conditions such as prevail on the wharf in Townsville the heat does not affect in a constant manner the men working either in the hold of ships or on the wharf in the sun, so far as pulse rate and blood-pressure are concerned, but only causes a slight rise in rectal temperature and perhaps in pulse rate, which roughly varies with the level of the wet bulb reading.

(5) Med. Jour. Australia, April 16, 1921.

Industrial Fatigue and Ventilation. The latest report of the Industrial Fatigue Research Board is reviewed in the *British Medical Journal*, April 9, 1921.

The report, which deals with the practical use of the katathermometer as an indicator of atmospheric conditions from a physiologic aspect, is based upon observations made in a number of boot and shoe factories under varying conditions, and also, for purposes of comparison, in an aircraft doping room. The katathermometer, it will be remembered, was devised by Dr. Leonard Hill in the course of his researches into the subject of ventilation. It is designed to measure its own rate of cooling at a temperature approximately that of the human body, and has an alcohol reservoir in the form of a cylindrical bulb, a stem graduated in tenths of a degree from 95° F. to 100° F., and at the top a small bulb, which acts as a safety overflow when the thermometer is heated, and readings are taken with the "kata" used both as a dry bulb and as a wet bulb thermometer.

As the result of the investigations, which were carried out first under the direction of Prof. T. Loveday, M. A., and later of Prof. E. L. Collis, M. D., the report points out that an atmosphere which will help to sustain physical energy should be cool rather than hot, dry rather than damp, and there should be brisk air movement. Neglect of these conditions may cause physical disability and inefficiency.

Examination of summer and winter records taken at several factories suggests that systems of ventilation which are adequate in winter can not always insure desirable physical conditions under adverse outdoor conditions in summer.

An interesting section of the report shows the effect of clothing on skin temperatures, and the principle is illustrated that comfort during working hours can be enhanced by a more careful choice of clothing. Conversations with operatives showed that the heavy worker too often has the idea that profuse perspiration is a necessary consequence of his occupation, and he guards against chill by wearing heavy woolen garments which absorb moisture; but light clothing would be preferable

because of its effect in allowing the free circulation of air between the garments and the skin.

What Air Does to Us. E. Huntington⁶ says that the great principle that should govern our use of the air is that of the optimum. The optimum is the most favorable condition.

The chief atmospheric optima relate to (1) temperature; (2) purity; (3) movement; (4) humidity; and (5) variability.

Temperature undoubtedly comes first on both counts. The optimum temperature, taking the average for day and night together, is about 64° F. It may vary a little for individuals; age makes some difference; so does the climate in which people have grown up; and there appears to be a slight difference according to race and occupation.

This means that in the rooms where people live and work the temperature may range up to 68 degrees or down to 60 degrees; it should never, however, remain above 68 degrees any longer than is absolutely necessary. Higher temperatures impose a strain upon the heart and actually raise the temperature of the blood; their effect is like that of a mild fever.

It is well recognized that movement of air is highly important. Air that seems quite impure and foul, or that is too hot and moist does less harm when moving than does much better air when stationary. One of the great reasons why we are behind primitive man in our relation to the air is that he was not skillful enough to shelter himself from moving air, while we have developed the false idea that the air in our houses should be almost motionless.

Moisture in the air is important in three respects:

1. The human lungs function best and can most easily regulate the temperature of the body when the air contains about 5 grains of water vapor per cubic foot. This means a relative humidity of about 100 per cent. at a temperature of 56 degrees; about 75 per cent. at 64 degrees; about 65 per cent. at 70 degrees; and still less at higher temperatures.

(6) Nation's Health, May, 1921.

2. Under ordinary conditions moist air is less dusty than dry.

If the air contains the right amount of water vapor, the evaporation from the skin at temperatures of 64 to 68 degrees is relatively slight, yet, sufficient, and, as a consequence, people feel as warm in a temperature of 65 degrees within doors on a winter day as they do ordinarily at 70 degrees or more when the air contains only about one-fourth as much moisture as it should. In the same way, if the air of the right temperature contains the right amount of vapor, a gentle movement does not chill people as does a similar movement of dry air.

Variability of temperature and probably of other conditions appears to be highly important. So far as exact studies have been made, they show that while extreme variations may do harm, mild variations are distinctly stimulating.

Other atmospheric conditions, such as electricity and light, also play a part in determining the health of the nation.

State Supervision of Municipal Water Supplies. In considering this subject, H. A. Whittaker⁷ enumerates the following as some of the most common errors associated with his work in connection with water supplies in Minnesota.

1. The use of surface waters without treatment.
2. The use of surface waters with water-purification plants in localities where underground supplies are available and would have provided safer water.
3. The installation of water-purification plants by local authorities who have little or no understanding of the theoretical or practical side of the treatment, nor the difficulties attending the operation of these plants.
4. The installation of chlorine plants to treat water that can not be properly purified with chlorine.
5. The addition of chlorine to raw water as it enters a filtration plant rather than to the effluent after filtration.
6. The failure to keep on hand duplicate parts of important equipment of water-purification plants, espe-

(7) *Journal-Lancet*, Oct. 15, 1920.

cially the parts of chlorine apparatus that are likely to get out of repair.

7. The installation of by-passes around water-purification plants by which untreated water can be admitted into the system without passing through the plant.

8. The improper operation of water-purification plants by unskilled or inefficient operators and without laboratory control.

9. The location of wells, pumping equipment, exposed mains, reservoirs, filters, etc., where they are subject to flooding with surface waters.

10. The construction of pits around wells at the surface in which all or part of the pumping equipment is located. This applies especially to drilled wells.

11. The connection of any part of the water-supply system with sewers or drains which would make it possible for sewage or surface water to back up into the wells, well pits, or storage reservoirs.

Chlorination of Drinking Water. In a circular issued by the Ministry of Health of Great Britain⁸ some essentials for the rapid and efficient chlorination of drinking water are set forth as follows:

In order to be sure that all infective organisms are killed, the chloride of lime must be added to the water in such quantity that free chlorine will be available to the extent of at least one part per million of water. This will be effected by the preparation of a solution of chloride of lime consisting of one ounce of chloride of lime to one quart of water. This will suffice to treat 2,000 gallons of a water which does not contain an excessive amount of mineral or organic matter.

After the addition of the chloride of lime, the water should, if practicable, be allowed to stand in an open tank for four hours before consumption. If this can not be effected the taste may often be removed by the addition of a small quantity of permanganate, sufficient to produce a very faint pink color, which fades away in from five to fifteen minutes; or, so far as the chlorine taste is concerned, by the addition of a solution of sodium thiosulphate (the hyposulphate of soda used in photography) in small quantities.

(8) *Lancet*, Sept. 24, 1921.

In case of a heavily polluted water, the circular states that it is well to make sure that some free chlorine is present after the addition of the solution to the water. This can be ascertained by the starch and iodide of potassium test, which is particularly sensitive if the water is at a low temperature; the materials for this test can be obtained in the form of compressed tablets.

Disinfection of Water. W. F. Walker and R. W. Pryer⁹ report that when water has been exposed to ultra violet rays about 69 per cent. of the rays most efficient in bactericidal action are absorbed by it. These rays are about the 1860 Augstrom unit group. The water becomes radioactive for the time and by reason of this quality bacteria in it are destroyed as are bacteria added to it for a certain time after the exposure. In fact at the end of a two-hour period after exposure the number of bacteria per cubic centimeter was less in some cases than was the number present in freshly exposed water and water one hour after exposure. G. M. Fair¹ is quoted as having found that exposure to violet rays is more destructive to spores than it is to bacteria, by reason of the greater transparency of the former.

MILK

New British Regulations. Concerning milk announcement is made² that the Food Controller, on the advice of the Ministry of Health, issues licenses permitting and regulating the use of the designations "Grade A (Certified) Milk" and "Grade A Milk" in connection with the sale of milk produced and handled in accordance with prescribed conditions.

In order that a license to sell milk under the designation "Grade A Milk" may be granted, the following conditions must be complied with:

1. Herds must be tuberculin tested.
2. Farms must score at least 300 out of a maximum of 500 for "equipment" and "methods," of which 250 must be obtained for "methods."

(9) Amer. Jour. Pub. Health, August, 1921.

(1) Jour. Amer. Water Works Ass'n., May, 1920.

(2) Med. Officer, Oct. 30, 1920.

3. The milk must be cooled on the farm and be consigned in a sealed container, having a descriptive label.

"Grade A (Certified) Milk" is licensed to be sold where the foregoing and the following additional requirements are complied with:

1. The milk must be cooled and bottled immediately after production in bottles which have been sterilized by steam.

2. Every bottle must be covered with a suitable outer cap overlapping the lip of the bottle, and this cap must bear the name and address of the producer.

3. The milk on examination at any time before delivery to the consumer must not contain *Bacillus coli* in 0.1 c.c. (in each of two tubes), or more than 30,000 bacteria per cubic centimeter.

4. The milk must not be delivered to the consumer more than two days after the day of production.

Manural Pollution Shown by Anaërobic Spore Test. John Weinzirl³ reports further observation on the possibility of testing milk for manural pollution by detecting the presence of anaërobes. He at first called his test the "*B. sporogenes* test." But being convinced now that several species of anaërobic bacteria are present in cow manure, he has adopted the more accurate designation "the anaërobic spore test."

The test is made as follows:

From 0.5 to 1 c.c. of melted paraffine is placed in a 15 mm. test tube which is plugged with cotton and is sterilized either by dry or by moist heat. By means of a sterile pipette, 5 c.c. of the milk under test are placed in each of five tubes containing paraffine. The tubes containing the milk and paraffine are then placed in the Arnold sterilizer and heated to 80° C. for from 10 to 15 minutes. This treatment melts the paraffine, which rises to the surface, where it hardens on cooling and forms the anaërobic seal. The heat also expels oxygen absorbed by the milk, thus rendering anaërobiosis more complete. All the vegetative bacteria present in the milk are killed by the heat, only the spore forms remaining. The tubes are then incubated for three days at 37° C. If anaërobes are present, gas *will* be formed, which

(3) Amer. Jour. Pub Health February, 1921.

lifts the paraffine plug in the tube (Plate IX). Two positives out of five tubes condemns the milk as showing excessive pollution.

His observations seem to show that the anaërobic spore test is far superior either to the total count or visible dirt tests as an indicator of manural pollution in milk, and apparently it equals the *B. coli* test for this purpose. This is true only when the tests are made with the advantages equal for all of them. The advantages are rarely equal, however; the total count is subject to many disturbing factors, and is quite useless for this purpose; the visible dirt is readily removed by clarification or even careful filtration, thus rendering the test well nigh useless; *B. coli* multiplies in milk unless the temperature is held down, hence it may falsely indicate pollution; or it is killed by pasteurization when it fails completely. Since the major portion of our milk supply is now pasteurized, the anaërobic spore test must be used if this product is to be checked for pollution.

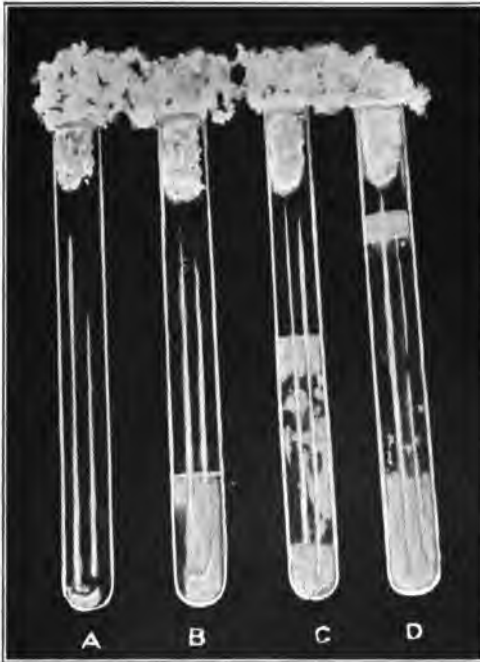
Milk Contamination. S. H. Ayres and P. W. Clemmer⁴ hold that the finding of *B. enterides pyrogenes* in ten tubes each containing 20 c.c. of milk is good evidence of contamination with cow manure. The Savage method in which ten tubes each containing 2 c.c. of milk are used is not satisfactory because the quantity used is not sufficient. The Weinzirl method of rating the cleanliness of milk by making use of a modified Savage method was not found satisfactory.

This reaction is known as the stormy fermentation. It is the phenomenon called putrefaction by the opponents of pasteurization who have spoken of it as occurring only in pasteurized milk. Pasteurization does not kill this organism and therefore the *B. sporogenes* test can be used to detect the probable contact with cow manure regardless of whether the milk has been pasteurized or not.

The sporogenes test is not dependable for use with one specimen but when applied to a number of samples from the same dairy it furnishes a fair criterion as to whether the methods employed were dirty or clean. It especially

(4) Bull. No. 940 U. S. Dept. Agriculture.

PLATE IX.



Illustrating the anaerobic spore test for manural pollution in milk. (A) Sterile tube containing paraffin; (B) Paraffin on top of the 5 cc. of milk; (C) Paraffin raised by gas formed; (D) Paraffin raised nearly to top of tube.—Weinziol, page 253.

indicates pollution with cow manure or its absence, and milking methods which introduce this agent or do not.

Use of Dried Milk. The use of dried milk in the tropics is considered at length in a paper by R. J. Blackham.⁵ He says that his own experience in India and during a visit to Ceylon showed that it was admirably adapted for the feeding of the youngest infant in the tropics.

He states that the French authorities and most municipal infant-welfare centers have found dried milk of special value in warm weather. All authorities have agreed that the product is especially adapted for tropical use. Harston, of Hong-Kong, has emphasized the advantages of dried milk over condensed milk.

Temperature Control as Related to Improvement of Milk. J. M. W. Kitchen⁶ of East Orange, N. J., in considering this subject concludes that the bad effects presumably produced by pasteurization are due to inherent bad qualities in milk prior to its heating, and to disruption of the proliferated bacteria in the milk; and that if good milk is heated moderately, no bad effects of the heating will be observed.

In general practice, the undestroyed residues of bacteria and spores in milk are allowed to grow because of the temperature at which milk is generally held during its distribution; and this is merely due to lack of temperature control.

What new practices then should be adopted? He thinks that some day in the distant future all milk will be preserved by holding it in insulated containers at temperatures sufficiently high to inhibit bacterial activity. In some warmer climates, milk is heated twice a day to preserve it. But in the present undeveloped stage of public intelligence, it will be better to hold on to intensely cold temperatures in controlling ferment action in milk, as well as in butter.

Rating a Milk Supply. The following method of evaluation of the Raleigh, N. C., milk supply was used as a basis of publicity by R. S. Dearstyne:⁷

(5) *Lancet*, Dec. 4, 1920.

(6) *Med. Record*, April 2, 1921.

(7) *Amer. Jour. Pub. Health*, August, 1921.

| Raw Milk | Points |
|--|--------|
| Sanitary or keeping quality..... | 60 |
| Bacterial count | 40 |
| Sediment test | 10 |
| Temperature | 10 |
| Equipment and methods of handling..... | 25 |
| Equipment | 7 |
| Methods | 18 |
| Nutritive value | 15 |
| Butter fat | 7 |
| Solids not fat..... | 8 |

If five original packages were collected and the four lowest counts averaged 25,000 or less 40 was allowed. For counts of 25,000 to 40,000 36 points; 40,000 to 60,000, 34 points; 60,000 to 80,000, 32 points; 80,000 to 100,000, 30 points; 100,000 to 120,000, 28 points; 120,000 to 140,000, 26 points; 140,000 to 160,000, 24 points; 160,000 to 180,000, 22 points; 180,000 to 200,000, 22 points; over 200,000, 10 points.

If four packages were cultured and the three lowest counts averaged 25,000 or less the allowance is 40 points; 25,000 to 40,000, 35 points; 40,000 to 60,000, 33 points; 60,000 to 80,000, 31 points; 80,000 to 100,000, 29 points; 100,000 to 120,000, 27 points; 120,000 to 140,000, 25 points; 140,000 to 160,000, 23 points; 160,000 to 180,000, 21 points; 180,000 to 200,000, 19 points; over 200,000, 10 points.

If only three packages are taken and plated use counts of all three and rate as on basis of five packages taken.

Score sediment as recommended in standard methods of milk analysis: To score perfect or 10 on temperature the milk must be delivered at 50° or under. Deduct 0.5 for every degree above 50.

In rating butter fat deduct 0.3 for every 0.1 of 1 per cent. below 4 per cent.

In rating solids not fat deduct 0.3 of 1 point for every 1 per cent. below 9 per cent.

In rating pasteurized milk, sanitary quality is given 70 points, of which bacterial count is 50 and equipment and methods 15, divided between equipment 5 and methods 10.

On other points the values are the same as those given raw milk. The ratings for bacterial counts is as follows:

Average of 15,000 or less 50 points; 15,000 to 25,000, 46 points; 25,000 to 40,000, 42 points; 40,000 to 60,000, 38 points; 60,000 to 80,000, 34 points; 80,000 to 100,000, 30 points; over 100,000, 20 points.

If eight specimens are taken the average of six lowest is to be taken; if six or seven, the average of five lowest; if five specimens, average of four lowest; if less than five, average of all.

[This method of rating like all other rating methods attempts to put on a rating basis by arbitrary methods subjects that can not be so translated with accuracy. In spite of this shortcoming, well-thought-out rating methods do good in that they stimulate competition. Dearstyne's rating of pasteurized milk as compared with raw milk could be interpreted as favoring either according as one detail or another was taken into consideration. In that it says that bacterial count is 70 per cent. of the whole in importance in pasteurized milk and 60 per cent. in raw milk it reverses the true relations. Since raw milk is more liable to produce pathogenic bacteria its count should be given the rating of 70 for approximate perfection.

In those places where 3 per cent. is the legal butter fat percentage it would seem that 1 point out of a possible 4 is not enough for a milk which conforms to law.—Ed.]

FOOD INSPECTION

Examination of Food Handlers for Tuberculosis.

M. J. Fine⁷ says that the efforts and expenditures in instituting such a system are vastly repaid by the results obtained. The city profits by limiting the spread of communicable disease and by detecting early and advanced cases of tuberculosis, many of which would have been discovered through no other source. The employe or food handler gains by an early diagnosis or knowledge of a condition present and, consequently, can resort to early treatment provided to restore him to health. The public at large benefits by the knowledge that food is being handled by individuals unable to disseminate any disease by contact.

(7) *Modern Med.*, March, 1921.

He reports 2,215 examinations made by the Department of Health, Newark, N. J., and 407 made by private physicians, or a total of 2,622. Of this number, 412 were suspected of having tuberculosis. Four were suspected by outside physicians. Fine points out that examinations are not readily submitted to and that difficulty is experienced in obtaining specimens of sputum.

Twenty-six cases of tuberculosis were diagnosed among the 282 submitting to re-examination.

Fine concludes that examination of food handlers for tuberculosis should be compulsory.

Bacterial Counts from Machine and Hand-Washed Dishes. R. S. Dearstyne⁹ points out that one of the

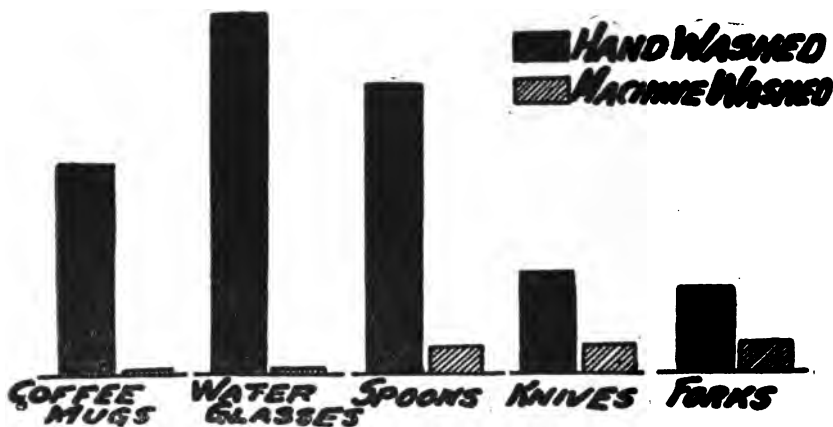


Fig. 22.

most potent sources of danger from the standpoint of sanitation in restaurant inspection is the matter of cleaning and handling dishes and utensils.

To determine what factors such dishes were in the spread of contagious diseases, he conducted a series of experiments to determine the degree of bacterial contamination remaining on dishes and utensils after various kinds of washing.

The germs left were washed or rinsed off into 100 c.c.

(9) Pub. Health Rep., June 10, 1921.

sterile water dilutions and plated in agar and counts read at the end of 48 hours' incubation at 37.5° C.

Figure 22 is a graphic representation of the average relative difference in bacterial count between machine and hand-washed dishes, from a numerical standpoint.

Examining for Spores *B. Botulinus*. K. F. Meyer and J. C. Geiger⁹ consider that examination of the stools of persons suffering from botulism for spores of *B. botulinus* is a valuable clinical diagnostic procedure. In botulism there is constipation due to inhibition of intestinal movement. This permits the retention of the bacillus. It is even possible that it may establish itself at least briefly in the intestine and continue to secrete poison. However, most observations indicate that the bacillus can be found only in that part of the intestinal content which represents the poisonous meal. The investigators recovered the organisms from the intestines and some of the other organs in individuals poisoned by eating some canned olive relish, by eating canned beets, and in two cases poisoned by eating canned spinach.

Oysters in Relation to Polluted Waters. According to T. C. Nelson¹⁰ the oyster crop of the United States is sold for \$15,000,000 a year. This is equal to 400,000 beeves. This crop is seriously threatened. For five years there has been no oyster seeding in the waters of Rhode Island, Connecticut and New York. If this continues a year or two more there will be no oysters produced in these waters. The oyster beds of New Jersey, Delaware, New York and the states south of there are not seriously threatened as yet.

Six hours after oyster eggs are fertilized they hatch into free swimming larvae. These move about in the water principally just below the surface for from fourteen to sixteen days according to the temperature of the waters. When two days old the larva develops two shells from which the swimming velum protrudes. At the end of the free swimming period, the young oyster attaches itself to something after which it remains fixed in its location, but feeding and growing by reason of

(9) Amer. Jour. Pub. Health, November, 1920.

(10) Ibid., June, 1921.

food and oxygen which it abstracts from the water which flows through its shell and into its organs.

The very great increase of pollution poured into the waters of the oyster beds during recent years has been a great menace to the oyster crop. In some instances the chemicals poured in have killed the oysters by chemical action. Acids and alkalies are particularly harmful. Minerals are sometimes carried long distances. Oysters containing from ten to twenty times the normal proportions of copper have been found long distances from where copper pollution had taken place.

Oiling of the waters kills the oyster larvae which swim just below the surface and also kills the vegetable and animal life on which oysters feed. If the amount of sewage in water is excessive it uses up the available oxygen and thus suffocates the oysters and also suffocates the life on which the oysters depend.

What is called the biologic machine in waters is a complicated mechanism. The sewage and the soil contribute nitrogen and organic matter. Vegetable life builds this to higher forms. Animals feed on this and higher animals feed on them. Once a link in this chain is broken the entire chain will go to pieces. Through the loss of oysters and other water-produced food this may be a source of great waste. Nelson says that the very great pollution by sewage and trade wastes of tidal waters on the Northern Atlantic seaboard is cradling this section in a septic tank and this in from ten to fifteen years will be a huge menace to the public health unless something to correct it is done.

Evaporating Fruits and Vegetables. W. V. Cruess² reports an investigation of methods of evaporating fruits and vegetables and the products both when sun drying and artificial heat drying were employed.

Grapes can be satisfactorily dried either by exposure to sun or by evaporation with hot air. The grapes are dipped in one-half ounce of 1 per cent. solution of lye at 100° C. for 5 seconds and then rinsed in water. Sulphuring for one-half hour is used for white grapes but not for red or black where evaporation is to be done.

It is continued for three hours if sun drying is to be employed.

Apricots preserved by evaporation were superior to the sun-dried product. Evaporated pears were superior to sun-dried pears in flavor and cooking quality but were inferior in appearance. The fruit is sulphured and dried in hot air with a humidity of 40.

Peaches are lye peeled and evaporated in hot air with a humidity of 25. The product was superior to the sun-dried product.

Evaporated prunes were superior to sun-dried in appearance and flavor.

Figs should be allowed to dry partially on the tree and the process continued by evaporation.

Berries, bananas and apples are successfully evaporated.

Vegetables, with the exception of asparagus and tomatoes, are successfully evaporated. The product is much superior to the sun-dried product in appearance, flavor and cooking qualities. Blanching in water or steam is preferable to sulphuring. Evaporated vegetables must contain less than 22 per cent. moisture to keep them from fermenting or developing molds. The best moisture content is 8 per cent.

Evaporated vegetables must be marketed in hermetically sealed containers. The best method of preventing the development of insects is to heat to 140° F. and to seal hermetically while the product is hot. Cruess holds that canning vegetables is an unjustified waste of tin and metal, and causes unjustified expense for transportation and other handling.

CHILD HYGIENE

Value and Interpretation of Physical Measurements.

Of recent years two particular methods of measurement, devised to assist in the assessment of physical condition, have been developed by medical physiologists: (a) The comparison of the vital capacity with the dimensions of the body devised by Professor Georges Dreyer; (b) the measurements of expiratory force and breath-holding as suggested by Wing-Commander Martin Flack.

C. B. Heald and B. Thomson,³ after a study of these tests in about 124 cases examined by the same instruments and the same examiners, conclude that the results show satisfactory evidence of the value of both the Flack and Dreyer tests. It is not to be expected that in so complex a mechanism as the human body simple and direct mathematical correlation of divers measurements can be obtained. The graphical method of correlation that the writers put forward for the Flack and Dreyer tests is almost incapable of formulative expression; it forms a modification of methods well known in thermodynamics and other branches of engineering. The writers believe that the application of these methods to anthropometry is new; they believe them capable of great extension, and that there is even some hope of obtaining them as useful efficiency factors for all the principal systems of the human body.

Nutritional Work in Schools. Katherine B. Rich⁴ in two papers sums up her studies of nutritional work in connection with 494 children in eight Chicago public schools.

Fifty per cent. of the school children who were weighed and measured were found to be below normal in height and weight for age, or in weight for height. She thinks these figures would approximate the findings in other localities, in all probability.

The work indicates that the undernourished children may be divided into three groups: (1) infants and young children up to the age of six years; (2) children from 6 to 13 years, and (3) boys and girls from 13 through the period of high school education.

The handling of the first two groups is an expensive undertaking, requiring the absolute coöperation of the parents, and consequently many visits of a capable worker. Organizations outside the school system seem best able to cope with these groups. The third group, on the contrary, is controlled almost exclusively through the proper presentation of the problem to the individual student, and through his own interested effort to become both physically and mentally fit. It is largely a

(3) *Lancet*, Oct. 9, 1920.

(4) *Jour. Amer. Med. Ass'n.*, Nov. 27, 1920, and April 9, 1921.

question of psychology, and presents a great opportunity for character building.

The nutritional worker has little effort to expend in reaching parents, as the children prefer to consider it their own business—their first real “job” in life—and get the coöperation at home when they feel the need of it.

Effect of Diet on Development of Teeth and Jaws. May Mellanby⁴ reports the results of experiments on puppies. To the basal diet, consisting of skim milk, yeast, orange juice, white bread, sodium chloride, and sometimes lean meat, were added the substances tested on the two groups.

When cod-liver oil, whole milk, butter, animal fats, except lard, some vegetable oils and egg yolk were added to the diet the puppies generally developed beautiful teeth and normal jaws.

On the other hand, when linseed oil, babassu oil, some other vegetable oils, extra separated milk, lard, sugar, rice, oatmeal or egg whites were added, defects of the jaws and dentition resulted.

The findings suggest to the author that a vitamine, either identical with fat-soluble A, or having a somewhat similar distribution, normally controls calcification processes in the teeth and jaws, the results of its absence being defective calcification.

School Ophthalmic Work. N. B. Harman⁵ holds that an educated and observant teacher is the first line of defense in protecting the child from the strain arising out of its inherent disabilities.

There appears to be no reason why an initial test of vision should not be done by the teachers; it would give them a knowledge of their charges that they would not otherwise obtain, and it would accentuate their interest in the conservation of child sight. It is likely that an educational arrangement based on a real knowledge of the condition of the children's eyes and the correction of the gross defects at an early age would tend to check the onset of much of the myopia developing in later years. Many of the defects found are not completely

(4) Med. Officer, May 28, 1921.

(5) Brit. Med. Jour., May 28, 1921.

susceptible to full correction, and the remaining defect may be one that requires special arrangements for the satisfactory education of the child.

About 2 per cent. of children in the schools suffer from blepharitis and conjunctivitis. In many of these the need is for regular and efficient cleansing.

The care of spectacles may be materially advanced by a routine parade of all children wearing them, at stated intervals.

There are a number of children, averaging about 2 per 1,000 of the school population, whose vision is too bad for them to take advantage of the ordinary curriculum.

Mental Health of Children. Glenn E. Myers⁶ concludes that the importance of heredity lies chiefly in a good physical condition, and in a normal capacity for intelligence; mental instability of the parents need not continue in the child if the environment is good from time of birth. By good environment Myers means not only proper food and cleanliness, but more specifically the attitude of the parents and other near relatives in relation to the child. The most desirable type of personality is the "open make-up." The only child, or the sickly child, is especially prone to the "shut-in" type of make-up, because its parents are apt to give it too much love, attention and indulgence, at the same time keeping it too much away from contact with the world, and thereby rendering it tender and unfit, and interfering with the full development of the personality. Such a child is liable to form too strong an attachment to a parent, which engenders a poor adaptation to sex, and directly affects its future happiness and efficiency and its usefulness to society. It should be permitted to spend most of its time with other children, of its own age, and of both sexes. Through such association the child develops instincts and acquires good habits, which will make him a happy man and a useful citizen.

Questions about sex should be truthfully answered, without postponement, but telling each time enough to satisfy and to insure a return to the same source for

further information. Masturbation is to be regarded as a normal phase of sexual development, but becomes abnormal when it persists, as a preferable form of sexual gratification, after a time when sexual interest should be transferred to the opposite sex. The child should not be allowed to believe that masturbation will lead to insanity. Traits known as "gentle" depend mainly upon the conduct of the parents in the presence of the child, therefore, the parents should consistently set the example before the child, of what they are or wish to be.

The basis of the entire future personality is formed in infancy and early childhood, and during these years the best effort should be made by the parents to furnish the proper environment. The development of the make-up should be closely followed in order to determine what trend the child's abilities take, and to educate him along that line.

Relation of Hospital Service to the Child. In an essay on the subject, Henry D. Chapin⁷ states that hospital social service should find both its best inspiration and highest development in the case of the child. Children, and especially infants, do not respond well to prolonged hospital care. As soon as acute symptoms of disease have passed they should be discharged. After many years of observation within and without the hospital he believes that a great number of cases of illness in young children can be treated better at home, if proper nursing is procurable.

We must not overlook the educational value to the home of good nursing service, as the mother can learn much as to the future care and nursing of her family from these visits. In this way, it is possible to raise the whole standard of living. If every infants' or children's hospital would thus reduce its inside work to a comparatively small unit, retaining its full medical and nursing staff to operate largely in the homes that supply the hospital, the best and most far-reaching results would be obtained, with the least expense.

Thyroid Enlargement in School Children. Herbert Sheasby⁸ reports that in Cardiff, of the 12,013 children

(7) Jour. Amer. Med. Ass'n., July 23, 1921. Digitized by Google

(8) Med. Officer, Aug. 13, 1921.

examined sixty-seven were found to have well-marked enlargement of the gland, *i. e.*, 0.55 per cent. This figure compares favorably with those published by other school medical inspectors where records have been kept. For example:

| | | |
|------------------------|------|-----------|
| Leicester (1919) | 1.8 | per cent. |
| Derby (1918) | 1.7 | per cent. |
| Northampton | 0.53 | per cent. |
| Cheshire | 8.0 | per cent. |
| Bath (1918-1919) | 1.0 | per cent. |

Of the twenty-three goitrous children treated, all can be said to have benefited. The earlier the case, the more marked the improvement, that is when treatment is given before fibrosis and cystic changes have supervened.

Incidence of Goiter in Wisconsin. R. C. Blankinship⁹ reports that examinations of 13,796 entering students at the University of Wisconsin, covering the years 1910 to 1917, inclusive, showed demonstrable thyroid enlargement in 3,874 cases, or 28 per cent., and exophthalmic goiter in ninety-three cases, or 0.6 per cent. Of the total number (13,796) examined about 70 per cent. were from Wisconsin, 20 per cent. from neighboring states, and the remainder from more distant states and foreign countries.

Age and sex incidence was as follows:

Male—

| | | |
|--------------------------------------|------|-----------|
| Simple unclassified enlargement..... | 21.9 | per cent. |
| Exophthalmic | .29 | per cent. |

Female—

| | | |
|--------------------------------------|-----|-----------|
| Simple unclassified enlargement..... | 41. | per cent. |
| Exophthalmic | 1.2 | per cent. |

Average combined age: 19.9 years.

Mortality statistics show that the average death rate in Wisconsin for the past five years from goiter is 2.4 per 100,000, while that for the entire United States for the corresponding time is 1.6 per 100,000.

From an intensive study of 300 cases of simple goiter, selected from the student examinations made in the fall of two different academic years, 1917 and 1918, the following interesting observations were made:

(9) Wis. Med. Jour., April, 1921.

Some abnormality of the upper respiratory tract or teeth was noted in 95.6 per cent.

Thirty-seven girls and nine boys, a total of 15.3 per cent., for one reason or another, were unable to carry on the prescribed course in physical training at the university. While the actual morbidity in terms of days lost has not been calculated for this group, it is obviously a great deal in excess of that observed for the entire student body.

Prevention of Simple Goiter. In 1917 David Marine and O. P. Kimball¹ began their work of preventing goiter in the school population of Akron, Ohio. The method consisted in the administration of 2 gm. of sodium iodide in 0.2 gm. doses, distributed over a period of two weeks, and repeated each autumn and spring. They say that the amount of iodine given is excessive and far beyond the needs of the individual or of the ability of the thyroid to utilize and store it. One gram distributed over a longer period would be better.

The results of two and one-half years' observations on school girls in Akron are as follows:

Of 2,190 pupils taking 2 gm. of sodium iodide twice yearly, only five have developed enlargement of the thyroid; while of 2,305 pupils not taking the prophylactic, 495 have developed thyroid enlargement. Of 1,182 pupils with thyroid enlargement at the first examination who took the prophylactic, 773 thyroids have decreased in size; while of 1,048 pupils with thyroid enlargement at the first examination who did not take the prophylactic, 145 thyroids have decreased in size. These figures demonstrate in a striking manner both the preventive and the curative effects.

The authors found that the dangers of giving iodine, in the amounts indicated, to children and adolescents are negligible. Exophthalmic goiter and iodism are the two important conditions to be looked for. They are of the opinion that most of the untoward effects recorded are due to the excessive doses employed.

Importance of Focal Infection. F. H. Wetmore² is of the opinion that much attention should be given in

(1) Jour. Amer. Med. Ass'n., Oct. 1, 1921.
(2) Can. Med. Ass'n. Jour., January, 1921.

school medical inspection to the detection of sources of focal infection. He states that at the Forsythe Dental Infirmary 40,000 abscessed teeth were found in 50,000 children examined.

Greatly enlarged tonsils and adenoids in the child should be removed so that the sinuses may be better drained, and be less likely to become diseased.

He says that C. K. P. Henry³ claims that after the correction of dental defects many tonsils regain their physiologic function, and become a dam instead of a sieve for bacteria.

Von Pirquet System of Nutrition. During the war von Pirquet, of Vienna, and his assistants, in attempting to solve the problems of nutrition resulting from the shortage of food supplies, worked out a system of feeding which has since attracted considerable attention.

An important feature of the system is the substitution of the "nem" as a unit of food value for the calory. The "nem" represents the food value of one gram of mother's milk, containing 1.7 per cent. proteid, 3.7 per cent. fat, and 6.7 per cent. carbohydrate.

The "nem" values of various foods as determined by von Pirquet are given by him in his *System der Ernährung*, published in 1919, together with a discussion of nutritional standards and their application to feeding methods. These standards and methods are all based on strict mathematical formulas, are an important part of the system, and are fully as essential as the new unit of food value, namely the "nem."

Mayerhofer and von Pirquet in 1920 published an excellent epitome, wherein the various details of the system and their application are described by them and their assistants. The essential facts and methods of the von Pirquet system are summarized by W. E. Carter⁴ as follows:

Von Pirquet believes that the sitting height is a basis for the more accurate estimation of the nutritional state than is the standing height. It was demonstrated that the cube of the sitting height in centimeters is approximately ten times the weight in grams, of the normal

(3) Can. Med. Jour., July, 1920.

(4) Jour. Amer. Med. Ass'n., Nov. 12, 1921.

person. With this formula in mind, it becomes easy to compute the nutritional state in percentages, when the sitting height and the weight are known. The formula would read:

$$\frac{10 \text{ times the weight}}{\text{Sitting height } \sqrt[3]{\quad}} \text{ equals 100 per cent.}$$

or

$$\frac{\sqrt[3]{10 \text{ times the weight}}}{\text{Sitting height}} \text{ equals 100 per cent.}$$

It is obvious from this formula that if the weight is lower, the percentage of nutrition (*pelidisi*) would be lower; and if the sitting height were higher, the percentage of nutrition likewise would be lower. In order to make a convenient term to designate this percentage of nutrition, von Pirquet coined the word "*pelidisi*" (*pondus, decies, linear, divided by sitting height*).

In actual practice the *pelidisi* of a well-nourished, normal child is very close to 100 per cent. An obese child may go up to 110 per cent. Thin children run between 88 and 94 per cent.

In order to verify the accuracy of the *pelidisi*, von Pirquet standardized the method of physical examination of the child. He classified the results of the examinations under four headings—*sanguis* (blood), *crassitudo* (fat), *turgor* and *muscularis*. He chose the vowel a to indicate normality, and e, i, o, u as symbols to designate the degree of deviation of these tissues above or below normal. In this way a new word was evolved, one that would represent the physical status of the child. Eventually "*sacratama*" came to mean the physical examination.

TABLE I. SACRATAMA

| | Sanguis (blood) | Crassitudo (fat) | Turgor (water) | Mucularis (muscle) | |
|---|--------------------|---------------------|-------------------|-----------------------|----------------------|
| i | Si | eri | ti | mi | Greatly increased |
| e | Se | cre | te | me | Moderately increased |
| a | Sa | cra | ta | ma | Normal |
| o | So | cro | to | mo | Moderately decreased |
| u | Su | cru | tu | mu | Greatly decreased |

Index 3-2-1-0.

Further, to simplify the formula (it is sometimes difficult to remember without consulting the chart what "so-cre-to-ma" for example, means), an index was formulated: 3-2-1-0. To illustrate: If a child were slightly anemic and moderately thin, but of good turgor and muscle tone, his classification would be "so-cro-ta-ma." It is apparent that there are two points off normal, so a circle is thrown around the 2. If, on the other hand, he were particularly well muscled and he were classified "so-cro-ta-me," he would have two points below normal and one point above; the difference would be 1, and a circle would be thrown around this number.

It is a common observation that there is a direct relationship between the pelidisi and the sacratama. When the pelidisi is around 90 per cent. the sacratama is likely to be three points off normal; if the pelidisi is near 95 per cent. the sacratama will probably be one or two points off normal. A normal pelidisi almost invariably accompanies a normal sacratama.

Von Pirquet felt that the calorie, which is a unit of measure best adapted to the requirements of the physicist and the engineer, does not meet the practical needs of the physician and dietitian. In place of the calorie, Pirquet prefers a nutritional unit based on the food value of 1 c.c. of milk. This unit he calls a "nem" (*nutrition-element-milk*).

Von Pirquet believes that there is a direct relationship between the food requirements of the individual and the "absorptive surface" of the alimentary canal. He demonstrated that the measure of this "absorptive surface" in square centimeters is equal to the figure arrived at by squaring his sitting height. Thus, a child with a sitting height of 50 cm. would have an absorptive surface of 2,500 square centimeters. It was further observed that, in twenty-four hours, this absorptive surface could not utilize more than 1 c.c. of milk or its equivalent in other food, for each square centimeter of its surface. Although the child in question could absorb a "maximum" quantity of 2,500 c.c. of milk (2,500 nem), or its equivalent in other food, the constant take of so much would tend to overtax the digestive system;

so that a lesser or "optimum" amount of food would be desirable.

He also estimated the needs of the individual for basal metabolism which is, of course, an irreducible "minimum," as three-tenths of the "maximum." The author of the system insists that the growing individual needs one-tenth of the calculated "maximum" for purposes of growth; that he must have another tenth for the maintenance of his reserves of body fat; that he requires still another tenth to meet the demand of moderate exercise and a further tenth if he is one whose activity is unusual. The sum of these fractions provides the physician with a basis for calculating the nutritive needs of the child and for writing his prescription. For example, the prescription would read, 0.5, 0.6, 0.7 or, unusual cases, 0.8. For these figures, Pirquet has given the name "decinemsiqua" (written DnSq).

The dispensing of this prescription becomes simplicity itself. The dietitian or nurse takes the sitting height of the child, squares it, and in this manner arrives at a figure that is identical with the number of square centimeters of "absorptive surface" of the individual's intestinal canal; it will be remembered that this figure also represents the maximum amount of food in nem, utilizable by the intestinal canal; and that to administer this "maximum" amount would derange the digestive system. She then notes by the prescription that the physician has prescribed but six-tenths of the maximum (written 6 DnSq). So she multiplies the square of the sitting height by the fraction prescribed, and the result gives her the daily total of food requirements. The von Pirquet method in no way interferes with proper "balancing" of a ration between its fat, carbohydrate and protein elements. Quite the contrary, it simplifies the estimation. In Table 2, "The Nem Value of Food-stuffs," a figure may be noted under the protein column. This represents the approximate amount of protein in dekanem (10 nem) contained in each hectonem (100 nem). For example, fresh ham carries 8 dekanem, or 80 nem, in each hectonem, of food value. So at the end of a daily menu, it becomes an easy matter to add up the dekanem of protein contained and to compare this

with the total number of nem prescribed. Von Pirquet estimates that at least one-tenth of the daily food ration should be protein in order that the "structural" element of the diet may be sufficient.

Outside the question of fat-soluble vitamins and the palatability of the mixtures, the originator of the system concerns himself but little about the fats. He believes that the carbohydrates and fats are largely interchangeable as "combustibles."

TABLE 2. THE NEM VALUE OF FOODSTUFFS

| | Nem in 1 Gm. | Protein, Dekanem in Hectonem |
|-------------------------------|-------------------|---------------------------------|
| Meat: | | |
| Tallow | 13 $\frac{1}{3}$ | 0 |
| Lard | 13 $\frac{1}{3}$ | 0 |
| Bacon | 10 | 0.5 |
| Fat mutton | 5 | 2 |
| Fat beef | 4 | 3 |
| Lean beef | 2 | 6 |
| Lean mutton | 2 $\frac{1}{2}$ | 4 |
| Fresh fat fish (salmon) | 2 $\frac{1}{2}$ | 4 |
| Fresh lean fish | 1 $\frac{1}{4}$ | 8 |
| Gelatin (jello) | Ignore food value | |
| Ham | 5 | 8 |
| Milk and Eggs: | | |
| Condensed with sugar | 5 | 1 |
| "Evaporated milk" | 2 | 2 |
| Mother's milk | 1 | 1 |
| Cow's milk | 1 | 2 |
| Skimmed milk | 0.5 | 4 |
| Cream | 3 $\frac{1}{2}$ | 1 |
| Whole egg | 2 $\frac{1}{2}$ | 3 |
| Egg yolk | 5 | 2 |
| Heavy cheese | 6 | 3 |
| Dry cheese | 4 | 5 |
| Cream cheese | 2 $\frac{1}{2}$ | 6 |
| White of egg | 0.6 | 9 |
| Fats: | | |
| Butter | 12 | 0 |
| Oleomargarin | 12 | 0 |
| Suet | 12 | 0 |
| Salad oil | 13 $\frac{1}{3}$ | 0 |
| Lard | 13 $\frac{1}{3}$ | 0 |
| Cereals: | | |
| Rice | 5 | 1 |
| Rice, cooked | 1 $\frac{1}{2}$ | 0.3 |
| Wheat flour (or other) | 5 | 1 |
| Crackers | 5 | 1 |

| | | |
|--------------------------|------|-----|
| Zwiebach or toast..... | 5 | 1 |
| Barley, oats, wheat..... | 4½ | 1 |
| Wheat bread | 4 | 1 |
| Vegetables: | | |
| Dried vegetables | 4 | 2 |
| Potato | 1¼ | 0.5 |
| Green peas | 1 | 2 |
| Green beans | 0.5 | 2 |
| Carrots | 0.5 | 1 |
| Turnips | 0.4 | 1 |
| Cabbage | 0.4 | 1 |
| Cauliflower | 0.4 | 2 |
| Spinach | 0.4 | 3 |
| Tomatoes | 0.25 | 2 |
| Asparagus | 0.25 | 2 |
| Lettuce, cucumber | 0.2 | 2 |
| Sweets: | | |
| Chocolate | 6¾ | 0 |
| Cocoa | 6 | 1 |
| Sugar—a starch | 6 | 0 |
| Syrup | 5 | 0 |
| Honey | 5 | 0 |
| Jam | 3¼ | 0 |
| Fruits: | | |
| Grapes | 1 | 0.5 |
| Fresh fruit | 0.6 | 0.5 |
| Grape juice | 1.5 | 0 |
| Lemon juice | 0.6 | 0 |
| Other fruit juices | 0.7 | 0 |
| Dried | 3.3 | 0.5 |
| Nuts: | | |
| Nuts | 9 | 1 |
| Sweet almonds | 8 | 1 |

Carter, in order to determine the relative accuracy of the pelidisi and sacratama features of the system when applied to American conditions, examined 1,282 well children of the San Francisco schools. He used the same technique as that applied to the Austrian children, with the exception that the clothing was not removed, but a correction was made for this.

An analysis of his results shows that in a school in a poor district, 66 per cent. of the children show pelidisi of 94 per cent. or under (this is the lower limit at which von Pirquet regards a child as normal).

In a school in an industrial district there are but 45 per cent. of the children with pelidisi under 94 per cent., and there are 15 per cent. with pelidisi 100 per cent. or above.

In a school in a wealthy district 49 per cent. of the children have pelidisis of 94 per cent. or below, and 10 per cent. are 100 per cent. or above.

In an open-air school for tuberculous children wherein a well-balanced noonday meal is given, 52 per cent. of the pupils show pelidisis below 94 per cent. and none are 100 per cent. or above.

Carter believes that the v. Pirquet system is applicable to American conditions, especially those under which it may be desirable to feed children in considerable numbers. The method is desirable because it provides a simple, accurate and rapid method of estimating the nutritional status easily grasped by workers even without medical training, and it impresses them in a graphic way with the necessity of proper nutrition; it reduces the prescribing of the requisite food intake to a simple formula based on the sitting height as a constant, and it makes it possible, by the use of a single word, to make a record of the child's nutritional state, which may serve for comparison with the results of future examinations.

E. Krumbholz,⁵ in reviewing his observations on the v. Pirquet system of feeding, states that the nem method of food evaluation has the advantage of simplicity, especially for those working in dietetics, who are not able to deal scientifically with the older system of caloric values.

The ready application of the nem methods in determining dietetic values of milk mixtures in infant feeding is also emphasized by the author.

For these reasons Krumbholz believes that the nem system has a place in nutritional work.

INFANT WELFARE

Infant Mortality. Until recently it has been impossible to discuss on any accurate or satisfactory basis the infant mortality of any considerable portion of the United States. It is a matter of great satisfaction to everyone interested in the subject of infant mortality that at last there is well-established a birth registration area for the United States, and four annual reports on

(5) *Archiv. f. Hygiene*, vol. 90, 1921.

birth statistics of this area have been issued to date by the Census Bureau.

Geographical and Seasonal Variations of the Infant Mortality in the United States. This is the subject of a report by F. S. Crum.⁶ He figures the rates on what is termed the "Infant Mortality Index," which is the rate per 1,000 of estimated population under 1 year of age. This rate he considers probably as accurate, if not more so, than the "rate" as births are nowhere so completely reported as deaths and the variation in the completeness of birth reporting is considerable, even in the large American cities.

A comparison of the infant mortality indices of the years 1918 and 1919 for 46 cities shows almost universally lower indices for 1919. He is of the opinion that the higher rates of 1918 may, in part, have been due also to the influenza epidemic in the last four months of that year; also, that the lower rate of 1919 must have been, in part, due to the work of the Federal Children's Bureau.

A valuable part of the report consists of five charts showing the weekly fluctuations in the infant mortality indices for four geographical groups of cities.

Summer Diarrhea in London. John Brownlee⁷ presents a short synopsis of the work done during the last year by the statistical department of the Medical Research Council, of which he is director.

He is of the opinion that summer diarrhea was in the main (for its etiology must be multiple) not one disease but two, the epidemic of the first type having its maximum in late July or early August, and of the second type in September. The forms of the epidemics are different and also the duration, the first having a steep ascent and a rapid decline, the second a more gradual slope throughout.

From his statistical studies he concludes that till 1899 the first type was predominant. Before that date, the later epidemic was most marked in 1895. In 1907 it became predominant; the only year since 1907 in which the amount of diarrhea was anything comparable with

(6) Amer. Jour. Pub. Health, October, 1920.

(7) Lancet, Aug. 20, 1921.

previous experience was 1911. Even in such a very hot year as 1917 a very small epidemic of summer diarrhea occurred. In former times the deaths associated with such a temperature as occurred in that year would have been well over 200 a week.

It would seem, therefore, that the first type of diarrhea has become extinct, or nearly extinct, and that the later type alone survives.

Relation of Pediatrics to Public Health. Lafon Jones⁸ is of the opinion that 90 per cent. or more of the practice of pediatrics is, or should be, prophylaxis, and that 90 per cent. of our shortcoming is in just this field. He holds that the bottle-fed baby should be more or less of a medical curiosity.

He believes, also, that in early school life, physicians should recognize the mentally retarded and the feeble-minded child, the epileptic, the constitutional inferior and the child with the psychopathic personality.

Review of Child Welfare Work. Rena M. Crawford⁹ reviews the child welfare work in New Orleans and some foreign countries.

She reports that most efficient child welfare work is done in New Zealand. The whole island is divided into districts and each district has its public health nurse. Every expectant mother may receive instructions in how to care for herself and to prepare for her baby. Every mother may be taught how to feed that baby. Since 1905 New Zealand's infant death rate from gastro-intestinal diseases has been cut one-fifth, the rate in respiratory diseases has been cut in half, and it has made a beginning in the reduction of the mortality from early infancy. It now has an infant death rate of 45.

England's efforts to look after the health of her children during the war resulted in reducing her infant mortality rate to the lowest figure in her history. The chief methods she employed to lower her infant mortality were:

1. Compulsory notification of births within thirty-six hours.

(8) Amer. Medicine, March, 1921.

(9) New Orleans Med. and Surg. Jour., August, 1921.

2. Aid from the central government to the various local government boards. (The central government gave 50 per cent. of the amount raised by any local board to be used for approved infant and maternity work).

3. Publication by the government of a fixed plan for welfare work, including antenatal, natal and postnatal clinics.

4. Great increase of health visitors.

5. Great increase of welfare centers.

The author contends that the United States, as a whole, is not being looked after, but excellent child welfare work is being done in certain cities, New York, Baltimore, Washington and others. New York has succeeded in reducing her infant mortality from 111.6 per 1,000 in 1911 to 82 in 1919.

In New Orleans for the ten years before 1919, out of every 100 deaths reported in the city, from twenty to twenty-five were of babies under 1 year of age. The percentage was never less than 20 or more than 25. In 1919, the percentage of infant deaths fell from 20 or 25 to 14.8 per cent. That was the first year the Child Welfare organization had even a relatively sufficient number of nurses in the field.

Results of Breast-Feeding Campaign in Minneapolis.

The results of a campaign in Minneapolis to encourage breast-feeding is recorded by J. P. Sedgwick and E. C. Fleischner.¹ The work was done by the Breast-Feeding Investigation Bureau of the Department of Pediatrics of the University of Minnesota, in coöperation with the Health Department and Infant Welfare Society.

Every physician in the city was written to, and was invited to visit the university, where the purpose of the bureau was carefully explained. When it was not possible to communicate with physicians in this way, representatives were sent to explain to them the details of the problem.

Every mother was visited, usually within the first three weeks, by a social service worker, at which time the so-called "First Information" was obtained, and if any difficulty in nursing was apparent, the bureau immediately communicated with the attending physi-

(1) Amer. Jour. Pub. Health, February, 1921.

cian. With his permission the patient was visited promptly by a nurse and an effort made to correct existing conditions.

When the baby was 6 weeks old and every month

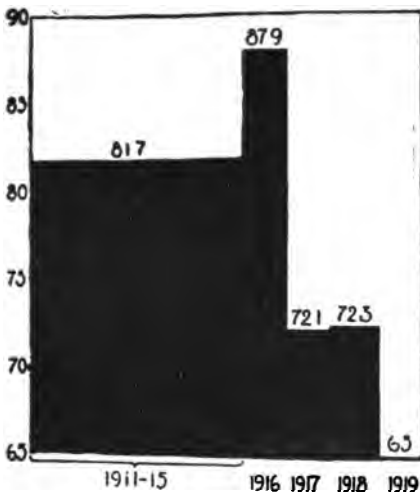


Fig. 28. Infant mortality in Minneapolis.

thereafter for nine months, there was mailed to the mother a card on which certain questions in regard to breast-feeding were asked.

A second call was made by the visiting nurse when the baby was two months of age.

The definite purpose of the Breast-Feeding Investigation Bureau was to reach the mother of every new-born baby in Minneapolis, and after the

confidence of the mother was secured, to educate her first in the value of breast-feeding and, second, in the means whereby it could be continued.

Analyzing the results of the investigation of the breast-feeding of babies born in Minneapolis during the months of January, February, March, April and May, 1919, the following statistics are available:

| End of | Babies Under Observation | Babies Breast Fed | Percentage on Artificial Food |
|-----------|--------------------------|-------------------|-------------------------------|
| 9th month | 2,022 | 1,472 | 27 |
| 8th month | 2,113 | 1,631 | 22 |
| 7th month | 2,240 | 1,810 | 19 |
| 6th month | 2,355 | 1,992 | 15 |
| 5th month | 2,412 | 2,090 | 13 |
| 4th month | 2,505 | 2,250 | 10 |
| 3rd month | 2,674 | 2,490 | 6 |
| 2nd month | 2,847 | 2,761 | 3 |

Naturally one must look for some tangible result from such startling figures, and that can very readily be found if the mortality rate of infants during the first year is studied. From 1911 to 1915 the infant mortality rate in Minneapolis was 81.7; in 1916, 87.9; in 1917, 72.1; in 1918, 72.3, and in 1919, the first year in which an extensive breast-feeding campaign was carried out, the rate was reduced to 65 (Fig. 23).

Health of Detroit Babies. In 1919, Detroit had an infant mortality rate of 96.7 and stood fifth among American large cities. St. Louis led this group of fourteen cities with a rate of 75.3. Since 1906, the Detroit infant mortality rate has fallen from 213. Nevertheless G. T. Palmer and G. A. Blakeslee,² dissatisfied with the progress made and the standing among cities of Detroit, analyzed the death rate to discover points for attacks.

They divided the city into about 200 zones and compared the death rates of babies in these. The highest rate was 216 and the lowest 15.1; sixteen zones had rates less than 50, sixty-three had rates over 50 and less than 100; the rates of forty-seven ranged between 100 and 150; rates of ten between 150 and 200; and two had rates above 200.

The highest rate among the racial groups was that of negroes, 151. Other racial groups were as follows: Greece, 149; Austria, Hungary and Bohemia, 119; Turkey and Syria, 112; Poland, 111; Belgium, 111; France, 109; Canada, 102; United States (whites), 95; Germany, 92; Denmark, Norway and Sweden, 88; Great Britain, 87; Italy, 85; Russia, 64.

A part of the difference in rates was due to economic factors, a part to other environmental influences and a part to differences inherent in the racial stocks. The Russian Jews had a low rate in great measure because they breast-feed their babies to an unusual extent. The same comment applies to the Italians. Other factors of importance in causing a low death rate were high family income, "mothers do not work out," low illegitimacy rate, absence of congestion of baby population.

Rather strangely Palmer and Blakeslee found "the

(2) Amer. Jour. Pub. Health, June, 1921.

greater frequency of breast-feeding among the Russian and Italians does not reduce their rate below that of the native whites where breast-feeding is relatively less common."

CONTROL OF CONTAGION

PNEUMONIA AND INFLUENZA

Pneumonia a Public Health Problem. The importance of pneumonia as a public health problem is discussed by G. C. Ruhland.³ He states that as a killing disease, pneumonia heads the list and that so far as the records of the Milwaukee Health Department are concerned, pneumonia has always been the cause for more deaths than any other communicable disease, tuberculosis not excepted.

The reasons why the public and professional interest has not been aroused on this problem and been lead to more definite action for the checking of this scourge, he attributes principally to the attitude of the medical profession toward the development of pneumonia as a disease arising within the patient himself. That is to say, it was assumed (and still is by many) that the organisms causing the pneumonia normally lodge on the mucous membranes of the healthy individual, and that under influence depressing to their human host, such as chilling the body, these organisms develop pathogenic properties and precipitate an attack of the clinically recognizable infection known as pneumonia. As a consequence of this attitude, little or no progress has been made in the control or prevention of the disease.

As measures for the better control of pneumonia, and for the lowering of the morbidity and mortality from the disease he recommends:

First, the prompt reporting of all cases.

Second, quarantine.

Third, bacteriologic determination of type of pneumococcus.

Fourth, the use of sheet and mask, and scrupulous personal cleanliness of attendant, and disinfection of all

(3) Wis. Med. Jour., October, 1920.

utensils used by the patient as well as the sterilization of the discharges from nose and throat.

Segregation of Pneumonia. The lack of efforts to segregate cases of pneumonia is commented on by T. S. Southworth.⁴ He is of the opinion that we may not have been sufficiently punctilious in taking measures to prevent the individual from becoming infected, and that one patent source that has not been sufficiently guarded against is the exposure of susceptible individuals in dangerous proximity to those having active cases of the disease.

He has repeatedly observed the incidence of pneumonia in wards quarantined for general outbreaks of measles, and also among groups of children who were segregated as they showed evidence of measles. Whenever pneumonia appeared among such children quarantined for measles, it extended rapidly with an appalling mortality.

Prevention of Respiratory Diseases. Based on his studies during the war of mess kits as a factor in the spread of respiratory diseases, Charles Lynch⁵ prefers to call these diseases "saliva-borne," instead of respiratory.

When the influenza epidemic struck at Newport News they had two groups of soldiers, one of which used mess kits which were washed in tepid water; the other group used table ware or washed their mess kits in boiling water. The consolidated tabulation shows the latter—the table-ware group—including the individual method but with boiling water, had a strength of 9,778 with 412 cases of influenza, and the former—the individual mess kits in tepid water—had a strength of 12,727, with 2,543 cases.

At Pig Point, Virginia, the civilians employed and the small ordnance organization, constituted 1,150 persons, and messed from table ware. Their rate of influenza for the 18-day period was 82 per thousand, with an average daily incidence of 4.5 per thousand. The two Fire and Guard organizations, whose strength was 445, ate from mess kits washed by the old line method.

(4) *Jour. Amer. Med. Ass'n.*, Oct. 2, 1920.
(5) *Med. Record*, Nov. 13, 1920.

In eighteen days they had 171 cases. In every respect the two Fire and Guard organizations were better off from the sanitary standpoint than the greatly overcrowded civilian group, save only in their method of washing their eating utensils.

From these observations he concludes that:

1. Influenza, as well as the other so-called air-borne or respiratory diseases, is essentially a hand-to-mouth infection.

2. There are major and minor modes of transmission by indirect contact—by the former through tepid mess-kit wash water, and by the latter through intermediate inanimate objects, the hand being the conveyor in both instances. Among troops approximately 75 per cent. of the cases arise by the major route. This applied to troop transports as well as camps.

Results of Protective Inoculation. G. B. Reed⁶ reports some results of protective inoculation in Kingston, Canada. The vaccine used contained several strains of four species combined and diluted as follows (with the addition of 0.5 per cent. phenol):

B. influenzae, 300 million bacteria per c.c.
Pneumococci, 100 million bacteria per c.c.
Green producing streptococci, 150 million bacteria per c.c.
M. catarrhalis, 50 million bacteria per c.c.

It will be seen that this vaccine contained a larger percentage of *B. influenzae* than the vaccine recommended by the British War Office Conference, and most of that used in the United States.

In the cases reported, the vaccine was used in two or three doses, as indicated, the first of 0.5 c.c. or 250 million, the second and third of 1 c.c. or 500 million organisms each, at forty-eight-hour intervals.

Table I. indicates the results of the use of this mixed vaccine with a group of 193 medical students. These inoculations were given before any cases developed among the number and before more than a half dozen cases had developed in the city, so that there had been little or no previous contact with cases.

(6) Can. Med. Ass'n. Jour., June, 1921.

TABLE 1. RESULTS FROM THE INOCULATION OF QUEEN'S MEDICAL STUDENTS WITH MIXED INFLUENZA VACCINE

| | Number | Per cent. |
|--|--------|-----------|
| Men in group not inoculated..... | 51 | .. |
| Cases of influenza among men not inoculated, period October 1st to November 30, 1918 | 22 | 45.3 |
| Cases of influenza among men not inoculated, period December 1, 1918, to January 31, 1919..... | 2 | 6.9 |
| Men in group given three inoculations.... | 142 | .. |
| Cases of influenza among inoculated men, period October 1 to November 30, 1918.. | 17 | 12 |
| Cases of influenza among inoculated men, period December 1, 1918, to January 31, 1919 | 10 | 8. |

Table II summarizes the results with the military personnel of this military district (M. D. No. 3). At the time of the epidemic there were several, mostly small, units in the district. Those inoculated were in Kingston, Ottawa, Cobourg and Deseronto. The inoculations were involuntary and were elected by about 18 per cent. of the officers and men in the several units. In most units the inoculations were given before any cases appeared; in others a few had developed before any inoculations could be given.

TABLE 2. RESULTS FROM THE INOCULATION OF PART OF THE MILITARY PERSONNEL, MD. NO. 3, WITH MIXED INFLUENZA VACCINE

| | Number | Per cent. |
|---|--------|-----------|
| Men not inoculated..... | 4,668 | .. |
| Cases of influenza among men not inoculated | 1,012 | 21.6 |
| Men inoculated, two or three doses..... | 907 | .. |
| Cases of influenza among inoculated men.... | 7 | 0.8 |

These statistics were collected by Major S. E. Thompson, formerly Sanitary Officer M.D. No. 3.

Table III contains the results of inoculation of about half of a group of 328 lumbermen divided among seven camps near Paisley, Ont. Approximately half the men in each camp were inoculated and half not inoculated.

TABLE 3. RESULTS FROM THE INOCULATION OF PART OF A GROUP OF MEN IN CAMP NEAR PAISLEY, ONT.

| | |
|--|-----|
| Number of men <i>not</i> inoculated..... | 175 |
| Number of cases influenza among men <i>not</i> inoculated..... | 47 |
| Number of deaths among men <i>not</i> inoculated..... | 7 |
| Percentage <i>not</i> inoculated who developed influenza..... | 29 |
| Number of men inoculated..... | 153 |
| Number of cases among inoculated men..... | 4 |
| Number of deaths among inoculated men..... | 1 |
| Percentage of inoculated who developed influenza..... | 2.6 |

Dr. James Kaliel gave these inoculations and kindly supplied the data contained in the table.

At the end of the epidemic, November 30, a questionnaire was sent to all physicians in Eastern Ontario who were supplied with the vaccine prepared in the laboratory. About thirty replied with as definite reports as could well be expected under such circumstances. These reports are summarized in Table IV.

TABLE 4. RESULTS FROM THE USE OF INFLUENZA VACCINE COMPILED FROM REPLIES TO QUESTIONNAIRE SENT IN BY THIRTY PHYSICIANS IN EASTERN ONTARIO.

| | Number | Per cent. |
|--|---------|-----------|
| Persons inoculated | 2,194 | .. |
| Cases of influenza among persons who received three or two inoculations..... | 104 | 4.7 |
| Cases among persons who received only one inoculation | 24 | .. |
| Total cases among persons who received one or more inoculations..... | 128 | 5.8 |
| Estimated number of cases of influenza among the general population of the several areas | 5 to 50 | per cent. |

From a study of these tables it appears that in the several groups of persons where part were inoculated with a mixed vaccine, *B. influenzae* predominating, there was a 22 per cent. influenza attack rate among the not inoculated and a 3.2 per cent attack rate among the inoculated persons.

Etiology of Epidemic Influenza. H. B. Maitland and G. C. Cameron,⁷ after a general review of the literature

(7) Can. Med. Ass'n. Jour., July, 1921.

on the causative agent reported during the last epidemic of influenza and a report of their experimental work, conclude that there is not sufficient evidence to indicate what is the cause of epidemic influenza. There is no experimental certainty that the virus is a filter-passer. The experiments which favor this view have been criticized in the light of results obtained in this laboratory.

B. influenzae is undoubtedly present in a large but varying percentage of cases, and is a factor in producing the pathologic complex of the disease. However, the failures to inoculate man form impressive evidence that it is not the primary infecting agent. The failure of animal inoculation and the absence of a pandemic strain are further facts in support of this view. The evidence favors the opinion that *B. influenzae* is a secondary invader.

The difficulties of making any advance in the problem arise mainly from the want of exact knowledge as to the essential lesions of the milder forms of epidemic influenza, and therefore of the lesions in animals which would indicate a reproduction of the disease.

Public Health Considerations of Influenza and Allied Epidemics. F. G. Crookshank⁸ states that it is the business of health officers to inquire why pestilences occur—to seek a way, if way there be, of foretelling their imminence, and to consider how far they may be prevented or modified by the means at our command, in the interests of the community as a whole. The inoculation, for example, of individuals during an epidemic, and the adoption of measures to limit contagion, are undoubtedly valuable, but they can no more prevent a pandemic of influenza than can gas masks and steel helmets prevent a war.

But, if the historical and epidemiologic methods of inquiry be pursued, even though they involve mental exercises abhorrent to the laboratory worker, we may hope to arrive more nearly at a true comprehension of the influenza problem than if we confine ourselves to purely pathologic investigation of individual casualties.

It is Crookshank's opinion that a pandemic of influenza is a coördinated series of happenings—in which

(8) Med. Officer, Oct. 2, 1920.

individuals and particular sets of circumstances play their part no doubt, but still, one ultimately caused by forces or agencies widely affecting the whole set of conditions of life upon this planet.

British Report on Influenza Epidemic. The medical department of the Ministry of Health has issued a report on the pandemic of influenza, 1918-19. The report is about 600 pages in length, and contains a vast amount of information.

The writer who deals with the subject of the epidemiology of influenza in this report, considers that possibly the influenza virus became virulent as the result of continued and frequent human passage in crowded places—that the overcrowding due directly and indirectly to the war intensified the virulence of the virus.

The chapter on the bacteriology of influenza is written by Sir Frederick Andrewes. He comes to the general conclusions that the disease is not caused, in all probability, by Pfeiffer's bacillus; and seems to favor the theory of the filterable virus of Nicolle and Lebailly.

Experimental Influenza. The results obtained by R. L. Cecil and G. I. Steffen⁹ confirm the results obtained by Blake and Cecil in their studies of experimental influenza in monkeys. In both instances the inoculation of virulent influenza bacilli usually caused an acute respiratory disease, similar in many respects to clinical influenza. Influenza bacilli were found in the discharges.

P. K. Olitsky and F. L. Gates¹ report the continuation of their studies noted in Volume III of this series, p. 289.

They state that from the filtered nasopharyngeal washing of patients in the first thirty-six hours of uncomplicated epidemic influenza and rarely later, they have cultivated a minute bacilloid body, *Bacterium pneumosintes*, from 0.15 to 0.3 microns in length, having definite cultural characteristics and capable of indefinite propagation on artificial media.

They also recovered the organism from the unfiltered and filtered lung tissue of rabbits and guinea-pigs in-

(9) Jour. Infec. Dis., March, 1921.

(1) Jour. Exper. Med., 1921, Vol. 23, p. 713.

oculated with unfiltered and filtered nasopharyngeal washings from early cases of influenza.

In rabbits and guinea-pigs, by intratracheal inoculations of mass cultures of this organism, they were able to obtain effects on the blood and lungs similar to those produced by the injection of nasopharyngeal secretions from influenza cases in the early stages. From the pulmonary lesions thus induced they recovered the same organism.

Further studies by the same authors² furnish additional proof of the identity of *Bacterium pneumosintes* and the active agent derived from the nasopharyngeal secretions in the early stages of epidemic influenza.

S. E. Branham and I. C. Hall³ during the winter of 1919-1920, examined fifty-five samples of nasopharyngeal washings from forty-four individuals, thirty-eight of the samples being from common colds, nine from influenza and eight from normal persons.

Their attempts to cultivate filtrable virus by the method of Foster showed no bodies in the "cultures" which could not be found also in those from normal persons or controls. It should, however, be noted that the influenza cases examined were not in the early stages.

TUBERCULOSIS

Retrospect and Outlook on Tuberculosis Problem.

Sir Arthur Newsholme⁴ in discussing this subject states that in childhood there is but little resistance to the infection of tuberculosis; and that if we are to reduce the amount of tuberculosis and to save children's lives, the prevention of exposure to infection during the first four or five and especially during the first two years of life is of supreme importance.

This inference from epidemiologic facts has an important bearing, both on general public health work and on special tuberculosis work. It emphasizes the importance of anxious and detailed care in respect to housing for tuberculous adults, including the provisions of

(2) Jour. Exper. Med., 1921, Vol. 24, p. 1.

(3) Jour. Infect. Dis., February, 1921.

(4) Med. Officer, May 14, 1921.

separate bedroom accommodation, either at home or in a hospital or sanatorium, if for no other reason, to protect young children from an imminent danger. This need for safeguarding the first two or three years of life from infection will remind the public health worker of the similar necessity for preventing children of the same age from acquiring measles, as it is then many times more fatal than later in life.

Minimizing the risk of infection especially for children is important, yet Newsholme is of the opinion that we can not hope in the complex circumstances of modern life to prevent infection entirely; but as the result of increased cleanliness in personal habits and of hospitalization of infectious cases on a steadily increasing scale, infection for most persons can be steadily diminished.

What we can hope to do, is to increase resistance to infection and prevent or diminish frequency and dosage of infection.

The principal factors making for or opposing reduction, he summarizes as follows:

Factors Making for Reduction

1. Gradual increase of small-dosed and infrequent in lieu of large dosed and frequent infection, and especially
 - (1) Increased cleanliness in personal habits (spitting, etc.).
 - (2) Reduction of dirt and of infection in industrial life.
 - (3) Better care of the sick.
2. Increased resistance by improvement of general hygienic conditions.
3. Provision of means for prompt diagnosis and continued treatment of tuberculosis. Dispensaries, residential institutions, open air schools, etc.

Factors Opposing Reduction

1. Steady increase of city life.
2. Increasing substitution of indoor for outdoor occupations.
3. The general reduction in house-room, especially in city life.

4. The evil influences of war on

- (1) Home workers.
- (2) Soldiers.

He states that measures taken against tuberculosis, direct and indirect, have been followed by a much greater reduction in this disease, than in the death rate from all other causes in the aggregate.

The terrible incidence of tuberculosis in infancy and the important part played by epidemic diseases in increasing tuberculosis emphasize the extreme importance of connecting tuberculosis work and child-welfare work closely together and of affiliating both to general public health work.

How Tuberculosis Schemes Fail. S. J. Maher⁵ is of the opinion that the failure of campaigns to reduce tuberculosis is in part due to the over-emphasis given to the value of the activities of the non-medical antituberculosis workers and the disinclination of most physicians to join heartily in a medical campaign dominated by non-medical functionaries.

Needed Change in Control of Tuberculosis. H. F. Gammons⁶ outlines certain changes that he thinks are necessary for the control of tuberculosis.

He says that 50 per cent. of the tuberculous, if they had known the early signs of this disease, could have sought the proper medical attention at a time when their disease was curable and would gladly have followed good advice. Therefore, he recommends repeated publication of the early signs of tuberculosis in the newspapers; also that schools for the education of physicians in all the up-to-date facts about tuberculosis should be opened in all sanatoriums.

He is of the opinion that there are a few tuberculous people who are considerate of the health of others, and that there should be places to send the careless and incorrigible consumptive, so that he will be under police control.

Criticism of Modern Opinions in Regard to Tuberculosis. A. Stewart⁷ says there is a general consensus

(5) Med. Record, Dec. 11, 1920.

(6) Tex. State Jour. Med., December, 1920.

(7) Med. Jour. Australia, July 30, 1921.

of opinion that there can be no activity in a diseased lung center without some rise in temperature. This rise in very mild cases may have to be looked for very carefully and in general practice is usually missed.

Another frequent mistake made is waiting in the absence of tubercle bacilli till signs of softening arise in the suspected lung.

Another condition which is well worth considering as it has not been appreciated by the profession, is the class of cases described by Fishberg of New York and called by him abortive pulmonary tuberculosis. The symptoms are most trivial, with an occasional cough, which is labelled, both to the satisfaction of the patient and his physician, as bronchitis or a cold on the chest. People in this condition with very little disability seem to live as long as other folk. It is in the terminal stages of this abortive form that keen practitioners often make an error.

After sixteen years of sanatorium work Stewart has found that patients having no rise in temperature, have a better chance of recovery than those who have; in other words, no fever days means high records of cure.

Also, he finds that in making the prognosis there is a common erroneous view that a good prognosis depends on the finding of a small number of tubercle bacilli in a microscopic field. He says that pathologically one tubercle bacillus is as good as a thousand. Temporary fluctuations are present in favorable and unfavorable cases and in acute cases they are frequently absent.

Factors in Control of Tuberculosis. Some of the fundamental factors in the control of tuberculosis are enumerated by H. Boswell⁸ as follows:

No campaign can be successful unless it is a part of a general health movement, coördinated with the various bureaus of the health department, subservient to the general health movement, and coördinated, further, with all welfare agencies and the Bureau of Animal Industry.

The sanatorium is the fountain head from which all this work should be carried on and through which public sentiment for the final work may be crystallized. The

(8) Jour. Amer. Med. Ass'n., Aug. 13, 1921.

sanatorium is a failure, so far as the prevention of the disease is concerned, unless it is operated as an educational institution rather than as a hospital.

A place must be maintained where indigent tuberculous individuals may be cared for during the remaining days of their lives, in order to protect an increasingly large number of the "non-immune" race from the dangerous carrier.

P. P. Jacobs⁹ says that much has been learned concerning the universality of infection with tuberculosis during the last five or six years and the optimism of the earlier days of the campaign against tuberculosis is giving way to dogged determination not to endeavor to eliminate tuberculosis within a few years, but to control the spread of the disease, as has been done with certain other infectious diseases.

Among the measures which he considers vital in any programme of tuberculosis control are the following:

The segregation of the infectious and communicable patient.

The education and treatment of the non-infectious individual by dispensaries, nurses, etc.

Traveling Tuberculosis Clinics. The work of the free demonstration and consultation tuberculosis clinics in Wisconsin is reported by Oscar Lotz and A. A. Pleyte.¹

These traveling clinics are maintained because the view is held that tuberculosis exists to a greater extent in a rural community than has generally been appreciated by physicians.

The object of the clinics has been mainly twofold: First, to discover tuberculosis in its early stages; second, to carry on an intensive, educational campaign. Which of these purposes is the more important, it is hard to venture a guess, for on one side by ferreting out the early cases of tuberculosis many lives are saved which would otherwise be lost, and many sources of infection are brought to light and placed under control. On the other side, through education, the danger signals of tuberculosis are made known, the object of the clinic is

(9) Calif. State Jour. Med., December, 1920.

(1) Wis. Med. Jour., February, 1921.

explained, people are urged to see their physicians earlier, they are urged to live rightly and they are taught the basic truths of right living; and also, physicians are taught the early diagnosis of tuberculosis and are stimulated to take a more active interest in tuberculosis health work.

Sanatorium Results. In this inquiry E. Ward² compares the condition of 270 sanatorium patients two years after leaving the institution with the condition of 597 controls two years after commencing treatment. To check the two-year results, a further series of 121 sanatorium cases, and 282 controls, is considered after a four years' period. The numbers are small because only cases seen by the author personally have been considered.

The patients are classified, as follows:

- Class 1. Patient at work—90 per cent. prospect of (c) or more.
(This may be considered a cure.)
- Class 2. Patient at work, but health somewhat uncertain—60-90 per cent. prospect of (c).
- Class 3. Working, but health precarious—40-60 per cent. of (c).
- Class 4. Too ill to work.
- Class 5. Very ill.

Of the 270 individuals in all stages of disease, two years after sanatorium treatment, 119 (44 per cent.) come under Classes 1 and 2; 44 (17 per cent.) under 3; 71 (26 per cent.) were classed as 4 and 5; and 36 (13 per cent.) were dead. It will be generally agreed that these are good sanatorium figures.

Tuberculosis Centers. What W. C. White³ calls the nucleus of the solution of the tuberculosis problem is a coördinated hospital and dispensary system located in the heart of a city and freely made use of for educational purposes. In Pittsburgh there is a tuberculosis hospital with 110 beds and a central dispensary with nine substations. In addition to caring for sick consumptives this institution gives courses of instruction to medical students, undergraduate nurses, graduate nurses, social workers and social visitors.

(2) Lancet, March 12, 1921.

(3) Inter. Jour. Pub. Health, May-June, 1921.

What about a Cure or Preventive for Tuberculosis? Based on his discussion of this question with many English and French leaders in tuberculosis work, and a study of the literature, S. J. Maher⁴ concludes that there is a spreading conviction that we will not make much further progress in the fight against tuberculosis until we have obtained a specific treatment for its cure or prevention, or both; and that in all probability this specific, when found, will be some live relation or modification of the tubercle bacillus.

Heredity in Tuberculosis. Karl Pearson⁵ states that in a community wherein tuberculosis has been prevalent for many centuries we should anticipate that natural selection would steadily intensify the immunity by eliminating those with less resistance; the higher grades of resistance survive and are transmitted by heredity. In a community wherein the tubercle bacillus has not been introduced there will have been no selection to raise the average degree of immunity; there will, however, be many grades of susceptibility; and these will be inherited, whether or no they have been put to the test of an infected environment.

The following facts were gathered from the data investigated in the Galton Laboratory:

There exists a correlation between parent and offspring in the matter of tuberculosis which is of the same intensity as the hereditary correlation between admittedly inherited characters in man.

The correlation between husband and wife in the matter of tuberculosis is far less intense than that between parent and offspring.

The earlier-born children appear to have a greater incidence of tuberculosis than later-born children.

The Soul of the Consumptive. S. A. Knopf⁶ says that the sufferings of the consumptive, rich or poor, man or woman, are not confined to the body alone. People will not employ even the recovered consumptive and some are afraid to touch him or associate with him. And yet, there is no more danger in association with

(4) Med. Record, May 7, 1921.

(5) Lancet, Oct. 30, 1920.

(6) New York Med. Jour., Jan. 1, 1921.

the consumptive who is conscientious in the disposal of his sputum than with any well person; therefore, Knopf counsels, let us treat him kindly and considerately.

Disinfection of Tuberculous Sputum. In summarizing their laboratory experiments with various disinfectants for tuberculous sputum, W. R. Stokes and C. H. Douthirt⁷ state that the custom of simply placing sputum in a 5 per cent. solution of phenol and expecting it to be disinfected in a short time is probably a dangerous procedure since it gives a sense of false security and the tuberculous sputum is not disinfected. The use of a 1 per cent. solution of coal-tar disinfectants, and perhaps other such disinfectants will destroy the tubercle bacillus in sputum if the disinfectant also contains 1 per cent. of caustic soda.

The authors also found that the Rideal-Walker or the Hygienic Laboratory phenol co-efficient used for testing the strength of a disinfectant has no direct bearing on its destructive action upon the tubercle bacillus in sputum, since the high co-efficients of these kresols would suggest that a very high dilution of the disinfectant should be used in sputum, and yet they find that it takes a 1 per cent. solution of kresol to cause the destruction of the tubercle bacillus in sputum.

Calmette's Protective Vaccination of Cattle. Theodore Shennan reviews the work of Calmette and Guérin first published in 1913 of immunizing cattle against tuberculosis.

Calmette and Guérin had observed that, by growing bovine tubercle bacilli upon bile-glycerine media through a long series of sub-cultures, they obtained a strain of attenuated bacilli which was non-pathogenic to cattle, monkeys and guinea-pigs. This strain was well tolerated by these animals even when injected intravenously in considerable doses, producing no tuberculous lesions, and conferring upon cattle especially, after thirty days, an immunity to virulent bacilli injected intravenously.

In a recent article by the same authors⁸ they report further experiments which tend to show that after 18

(7) Amer. Jour. Pub. Health, December, 1920.

(8) Ann. Pasteur Institute, September, 1920.

months of living in close contact with tuberculous cattle, six vaccinated animals were negative to the tuberculin test, whereas three out of the four controls were manifestly infected; the fourth control, which still showed a negative reaction, showing evidence of an individual resistance, even under conditions highly favorable to infection.

Calmette concludes from these experiments that his method of vaccination confers on cattle immunity to tuberculosis, not only when virulent bovine bacilli are inoculated experimentally, but also when the vaccinated animals live in close association with manifestly tuberculous cattle. The duration of the immunity produced by the vaccination is about eighteen months, but it can be renewed by revaccination yearly.

Shennan thinks that theoretically it should be possible to protect the young human beings from bovine infection by vaccination at stated intervals with avirulent bovine tubercle bacilli, prepared by some method such as Calmette's, but the procedure would have to be proved free from danger even to the weakest infant, and the dosage adapted to the varying natural or acquired susceptibility of different individuals, and different families.

Also, if bovo-vaccination, conducted according to Calmette's method, proved free from danger when applied to the human subject, and successful in affording protection from infection from bovine sources, it might be expected also to protect to some degree at least against infection from human sources.

And, further, if strains of virulent human tubercle bacilli could be rendered avirulent by treating them as Calmette and Guérin treated their bovine strain, they might be employed for protective vaccination, or even for therapeutic inoculation; but here again the difficulties of demonstrating the diminution of virulence would be even greater than in the case of bovine bacillus.

Control of Tuberculosis in Cattle. The campaign to control tuberculosis in cattle in Pennsylvania is described by C. J. Marshall.¹ The work was begun in 1896. During the period of twenty-three years from 1896 to 1919,

(1) New York Med. Jour. April 6, 1921.

272,895 head of cattle were tested with tuberculin under state supervision; of this number 32,392 head failed to pass the test.

The state has never attempted to force herd owners to submit their animals to a tuberculin test. Certain local boards of health have been rather insistent at times that the state should help them force a test on all animals producing milk for the community. The state has never been able or willing to do so. The best progress has been made in coöperation with the owners. Practically all testing has been done at the request of the owner after he had been fully informed of most of the disagreeable conditions that were likely to arise. There has scarcely been a time in twenty years when there were not many more applications for testing than the state was able to handle. With this same spirit of coöperation a few local boards of health have been able to get milk from tuberculin-tested cattle.

Breeders have had an opportunity for the past twenty years to make use of what has been known as the Bang system for controlling tuberculosis. Theoretically, the Bang system was considered quite ideal. In America it has not proved popular. It requires two sets of buildings. The owner is seldom equipped with sufficient stable and pasture room for more than one herd. He soon tires of having animals around that he believes to be diseased; his diseased herd is considered more or less of a menace in the neighborhood; in a sparsely settled community most people know that the herd is diseased and nobody wants the milk, even though it may be carefully and cleanly handled and properly pasteurized.

Bovine Tubercle Bacilli. That the bovine form of the tubercle bacillus is the supremely pathogenic type is the opinion of E. C. Schroeder.² It is responsible for tuberculosis in cows, in hogs and in children. Although hogs are infected from cows the bovine bacilli in them do not infect other hogs and they are not a source of reinfection of hogs. From the epidemiologic standpoint as regards cows, porcine infection is a blind alley. Likewise the bovine bacillus in the young human body multiplies but it does not infect other human beings. Nor is this a

(2) Jour. Amer. Vet. Med. Ass'n., July, 1921.

source of infection of cows. From the same standpoint it too is a blind alley. The cow is infected by infected cows. The infected cow infects other cows, pigs, human beings and other animals, the latter but rarely, however.

Every case of tuberculosis in human subjects due to bovine tubercle bacilli must be charged to intimate contact, in most instances through the ingestion of contaminated dairy products between persons and tuberculous cattle. The human tubercle bacillus while very important from the standpoint of human tuberculosis requires no consideration whatever in bovine tuberculosis eradication projects, since cows are immune to it.

Tuberculosis among hogs is unimportant except as it indicates the extent of tuberculosis among cows and the economic waste it occasions. Tuberculosis among fowls is due to the avian type of the bacillus. This bacillus does not cause tuberculosis among mammals nor can the forms of mammalian tuberculosis cause tuberculosis among fowls.

While the tubercle bacillus is in a certain sense capable of mutation in its type it is as nearly fixed and free from tendency to mutation as any bacillus of which we know. The small number of known types and the fixity of those types, their growth, peculiarities, the varying reaction of different animals and the epidemiologic factors in the diseases produced by them prove that the types are fixed to an exceptional degree.

CONTAGIOUS DISEASES

Sequelae of the Communicable Diseases of Childhood as a Public Health Problem. Isaac A. Abt,³ in discussing this subject, states that the specific nature of sequelae depends on the affinity that certain organisms have for certain tissues. Thus, we know what whooping cough and measles tend to produce bronchial disorders and to tuberculize the patient. A tuberculosis which has been latent in the body of the patient may be stimulated to activity, or possibly a new invasion of the tubercle bacilli occurs. In the same way, the toxins of diphtheria and tetanus show an affinity for the nerve

(3) Jour. Amer. Med. Ass'n., Aug. 27, 1921.

structures. The morbid effects of scarlet fever tend, for the most part, to produce kidney, nerve and cardiac lesions. Fifty years ago, the older clinicians thought that sequelae were new morbid processes of some unknown or mysterious nature engrafted on the original disease. It seems evident from recent studies and advances that sequelae of diseases are but a continuation in some form or another of the original infective process.

Abt points out that sequelae tend to establish a mortality rate which it is difficult to state in tables of vital statistics, and which, therefore, constitutes an unaccounted for death rate, as a result of the remote effects of communicable diseases. He concludes that the most valuable lesson to be learned from the study of the sequelae of the communicable diseases is the need to emphasize the disastrous results not only of the immediate, but also of the remote effects, and to urge upon all concerned the great importance of their prevention. The thought must occur to everyone that the most important factor in the prevention of the acute communicable diseases is the acquisition of more definite knowledge as to their cause and their mode of transmission. Experience has taught us that intelligent preventive measures can be carried on when exact etiologic factors or modes of transmission are known.

Control of Contagious Diseases. J. W. Bruce⁴ emphasizes certain points in the control of contagious diseases. The prevailing high death rate in diphtheria he attributes to the fact that antitoxin is not given early enough or in large enough quantities. In order to stop the ravages of diphtheria the antitoxin must be given almost as soon as infection takes place, for once the toxin has attached itself to nervous or muscular structures, the damage is done and all the antitoxin in the world cannot dislodge it. The great danger in diphtheria is from the heart and nerve complications. After the fourth or fifth day, and in virulent cases even after the second or third day, these structures may have been attacked and by that time antitoxin can only prevent further damage, but it can not heal the injury already inflicted. It is like calling the fire de-

(4) Kentucky Med. Jour. January, 1921.

partment after the fire has ruined the house. In a series of 1,047 cases of diphtheria at the contagious department of the Boston City Hospital, fifty-eight patients received antitoxin on the first day and not one died; 253 received antitoxin on the second day and the mortality was 0.8 per cent.; 239 received it on the third day of the disease, with a mortality of 5.8 per cent.; 176 received it on the fourth day, with a mortality of 9 per cent., and 110 on the fifth day, the mortality being 14 per cent. At this hospital there have been 460 cases of diphtheria among the doctors, nurses and employes since 1895, and there has not been a death, which is due unquestionably to the fact that antitoxin was administered in large doses at the outset of the attacks, often before a membrane had formed.

Bruce recommends that antitoxin should be given in an overwhelming dose just as soon as the clinical diagnosis is made and without waiting for the laboratory to confirm it. If we wait for the laboratory we lose at least from twenty-four to thirty-six valuable hours. This does not mean that we must not send a throat culture to the laboratory, for it is most important that we should in order properly to take care of contact cases, etc., but we must not wait for the report from the laboratory before we give antitoxin. It is perfectly safe to give more than enough; no symptoms can arise from overdosage, but it is very dangerous not to give enough. Antitoxin is best administered in one big overwhelming dose. If the injection has to be repeated a second time, it is an admission that enough was not given the first time. The purpose is to smother absolutely the toxin circulating in the blood, just as one would smother a fire with water. In cases of diphtheria of the pharynx and fauces, no matter how mild, the patient should receive 18,000 to 24,000 units because the toxic absorption from this area is so great and if there is much toxemia 48,000 to 75,000 units should be given. In the cases of laryngeal diphtheria the dosage need not be so large, because absorption of toxin is not so great and the danger is from mechanical obstruction; 18,000 units will usually suffice in these cases.

It has been proven conclusively that antitoxin in-

jected intravenously acts much more quickly than the same amount subcutaneously, and therefore it should be used by this method in very toxic cases where quick action is necessary. The subcutaneous antitoxin is almost as effective, but it takes some time to be absorbed into the circulation and it is a great advantage in severe cases to overwhelm the circulating toxin all at one time with an intravenous injection. With the concentrated antitoxin such as can be obtained through the State Board of Health, the bulkiness of serum medication can be greatly eliminated and thus a great difficulty in intravenous medication is avoided. With this preparation the doctor can give 1,000 or 10,000 units of antitoxin and still use the same quantity of serum.

Commenting upon the use of vaccine in whooping cough, Bruce states that the uses may be divided into prophylactic and curative. It is well established that vaccines are of benefit in prophylaxis. They are given at two-day intervals in three doses, one-half, one and two billion bacteria, respectively. There is almost never any constitutional reaction after the injections, *e. g.*, fever. Some very careful work has been done which goes to show that much better results are obtained with perfectly fresh vaccine (less than a week old) which contains no preservative.

Opinion is divided about the curative use of vaccines. No one is really enthusiastic about their results and the common feeling is that they certainly do no harm and may do some good. It is generally believed that vaccines do most good when given in the catarrhal stage of the disease before the paroxysms have begun. The difficulty arises here of diagnosing between the catarrhal stage of whooping cough and ordinary bronchitis and the author thinks it is good practice to give vaccines in any case of severe cough where there is an epidemic of pertussis or a history of exposure to it. The vaccine is commonly administered in four doses, at two or three-day intervals of one-half, one, two and four billion bacteria, respectively.

The Contamination of the Hands and Other Objects in the Spread of Contagious Diseases. This subject was studied at the Durand Hospital, Chicago, by W. J.

Matousek.⁵ He found that pathogenic bacteria present in the secretions of diphtheria and scarlet fever cases may be cultivated from the surroundings of the patient, but in the former disease less often than in the latter. Improperly sterilized eating utensils may readily serve as carriers of infectious material.

The thorough washing of the hands with soap and warm running water efficiently removes the secretions with which the hands may become contaminated. To facilitate this, the skin of the hands and nails requires special care in order to insure a smooth healthy surface and freedom from any local condition which may render thorough cleaning difficult or impossible.

Gauze masks protect the faces of the nurses from gross contamination with particles of air-borne secretions.

Cultures from the hands of attendants are a useful check on the individual technique of those caring for contagious diseases.

Cultural studies of the surroundings of patients with contagious diseases may serve to indicate the efficiency of the technic employed, and if applied at intervals they seem to stimulate attendants to greater efforts toward perfection.

DIPHTHERIA

Prevention of Diphtheria. J. H. Doupe,⁶ in summarizing the problem of diphtheria prevention, calls attention to the value of the Schick test and toxin-antitoxin immunization in the control of the disease.

He is of the opinion that diphtheria can be made as rare as smallpox and thinks that four years of experience with toxin-antitoxin immunization has demonstrated the truth of such an assertion. However, the information has spread slowly, and in many quarters this preventive measure is unknown or its use not understood. Therefore, diphtheria is still a widespread disease and the deaths from it are unnecessary sacrifices to ignorance. The mortality from diphtheria is high. The 1919 mortality census from the registration area in the

(5) Jour. Amer. Med. Ass'n., May 28, 1921.

(6) Journal-Lancet, March 1, 1921.

United States showed there were almost twice as many deaths from diphtheria as from measles or scarlet fever. So, in spite of the availability of the specific antitoxin, numbers die from a disease which can be erased from medical consideration.

There are many causes of high mortality. The two chief causes are delayed and insufficient treatment. Rachford states that less than 5 per cent. die if antitoxin is given in the first twenty-four hours, less than 10 per cent. in the second twenty-four hours, 20 per cent. in the third, and 40 per cent. in the fourth. The delay frequently depends on the insidiousness of the onset, particularly in the laryngeal and nasal types. A purulent nasal discharge may be mistaken for an ordinary pus infection in the nasal sinuses, and hoarseness may be ascribed to non-membranous croup. Too often small doses of antitoxin are used, which do not retard the progress of a virulent infection. The truth of the statement is very apparent that fewer deaths would result if antitoxin were made available in lots not less than 10,000 units each. Such a quantity is no more harmful than 1,000 units.

Another very important factor in mortality is age. The younger the child the greater the incidence of diphtheria, and the greater the mortality. Rachford, for instance, estimates that during the first year the mortality is 50 per cent., during the second year 30 per cent. and after the seventh year 7 or 8 per cent. The importance of the early period of life is further illustrated by Zingher's figures taken from the New York City Reports. From 1900 to 1917, 77.5 per cent. of deaths from diphtheria occurred in children under the age of 5 years. In the period from 1891 to 1900, when one might say diphtheria antitoxin was being introduced, the figures were 81.5 per cent. of the deaths were under five years. In other words, increased familiarity with and recognition of the value of antitoxin did not materially diminish the greater danger of diphtheria in the first few years of life. It is readily seen that any procedure which will reduce or obliterate diphtheria in the first few years will solve the problem of diphtheria prevention.

Campaign Against Diphtheria in Large Communities.

A systematic plan for the control of diphtheria in large communities is described by F. v. Gutfeld⁷ of the Medical Office of the city of Berlin.

He considers the education of the public the cornerstone of any plan of contagious disease control and says the first one upon whom this duty falls is the physician in attendance upon the case.

The immunization of contacts with antitoxin is recommended. If such individuals subsequently develop diphtheria and require additional doses of antitoxin, the danger of anaphylaxis can be overcome if antitoxic bovine serum is exclusively used for immunizing purposes and the horse serum is used for treatment purposes.

The author points out that the control of healthy carriers is still an unsolved problem; and also that v. Behring and Kruse do not consider the isolation of such cases practical, while Abel suggests that they should be isolated in institutions.

The control of diphtheria outbreaks in schools and institutions, Putfeld holds, should be entrusted to physicians and nurses assigned especially to this work, because this work can not be attended to efficiently and energetically enough by officials already over-burdened with a multiplicity of duties. In Berlin fourteen nurses are assigned specially to this work.

Diphtheria in Berlin. An epidemiologic study of diphtheria in Berlin is presented by E. Seligmann.⁸

In a comprehensive review of the history of diphtheria in Berlin and the measures employed for its control, he points out that the diagnosis "diphtheritis" first appeared on the death certificate as a cause of death in 1863. Since then, and especially in the last forty years, rapid advances have been made so that to-day diphtheria is bacteriologically one of the best known diseases.

The diphtheria mortality rate in 1883 was 233 per 100,000. In the next year compulsory notification by physicians was first made effective, following which the rate gradually went down, reaching 86 per 100,000 in

(7) *Offentl. Gesundheitspflege*, 6 Jahrg., 1921.

(8) *Zeitschr. f. Hyg. u. Infektionskrankheiten*, May, 1921.

1894, the year when antitoxin came into use. In 1896 the rate reached 33, dropping to 29 in 1900, and finally reached 17 in 1906. It is interesting to note that since that time the rate has not again fallen below 22. In fact, it reached 42 in the years 1911, 1915 and 1916.

In general, the figures show that from 1905 to 1914, diphtheria has increased in prevalence and has shown no marked reduction in its rate of mortality of those affected; this rate since 1909, during which year the mortality first fell below 10 per cent., being namely, 9.6 per cent. In 1913, 1914 and 1915 the mortality rates were 8.7, 8.2 and 8.3 per cent. respectively.

The figures presented show greater prevalence of the disease in the age groups 1 to 5, and 5 to 10 years or 107.4 and 111.9 respectively for these two groups, per 10,000 living in this group for 1905 to 1914.

On the other hand, the case mortality rate is greatest in the 0 to 1 year and the 1 to 5 year group, being 42.7 and 17.6 per cent. for these two groups respectively.

As to seasonal distribution, the figures show that the annual diphtheria cycle begins in August and ends in July, the highest rates for Berlin from 1905 to 1914 occurring in November.

The figures as to hospitalization show that the percentage of cases hospitalized runs in the neighborhood of 50 since 1891, and 56 and 55, respectively, in 1916 and 1917.

The author reports only on antitoxin as an immunizing agent. In a series of 7,952 immunized and 6,092 unimmunized diphtheria families, the disease occurred in 4.5 per cent of the former and in 19.4 per cent. of the latter group.

He says that the work on toxin-antitoxin was interrupted by the war.

Practical Value of Toxin-Antitoxin Injections and of the Schick Test. W. H. Park⁸ summarizes the practical value of the toxin-antitoxin injections in the immunization against diphtheria, and discusses the value of the Schick test as a means for identifying those who are susceptible to this disease. He points out that efforts during the last few years to further lessen the number

(8) Penn. Med. Jour., April, 1921.

of deaths and the amount of diphtheria by the more general use of antitoxin have been largely unavailing. Some of the reasons for this are plain. One of the chief ones is evidently the great number of healthy individuals who carry in their throats diphtheria bacilli. Careful investigations have revealed the fact that at any time during the winter more than 1 per cent. of the population are diphtheria-bacillus carriers and more than one-half of all cases of diphtheria develop in persons who have not been in known contact with the disease. Even if laboratories could make throat cultures from every one it would be impossible to isolate the number of persons detected and even those found to be free, at the time of the culture, would frequently become carriers during the period of investigation. The value of cultures for other than diagnostic purposes is largely limited to its use in families and institutions. The effectiveness of antitoxin as a general immunizing agent is limited because of the short duration of the passive immunity. To be effectual the injections would have to be given every three weeks. This is utterly impracticable as a general immunizing measure. We also have no prospects of so educating the public as to the necessity of the very early use of serum in treatment so as to save a much larger percentage than is now possible. Unfortunately, the therapeutic use must always be limited in its success because so many do not realize the nature and seriousness of the attack soon enough to seek early treatment, and because so frequently early complicating infections such as those due to the streptococcus and pneumococcus gain a headway which renders us powerless to prevent the development of bronchopneumonia or some other dangerous complication.

At the present time, we realize that, in spite of the wonderful results of the use of antitoxin, diphtheria is still a disease to be greatly dreaded. When the health authorities in New York City appreciated that we must expect each year about 1,200 deaths from diphtheria and 17,000 cases, they began seriously to think of the utilization of vaccination with a modified diphtheria toxin as a necessary public health measure. Active immunization, if successful, would have the great advan-

tage over passive antitoxin immunization of having a much longer duration.

Touching on some points in the practical application of the toxin-antitoxin treatment, Park attributes the reactions sometimes observed to the fact that the diphtheria toxin-antitoxin mixture contains, besides the neutralized toxin, a considerable amount of protein substance. This is partly formed of the proteins originally present in the broth in which the bacilli grew and partly from the autolyzed substance of some of the older bacilli in the culture. The reaction to the injection is similar to the typhoid vaccine but it is of less severity.

As to other factors he says that the element of age is very important. The infant in the great majority of cases shows neither local nor constitutional reaction, while among small children some 10 per cent. show a disturbance, and older children and adults, exhibit in perhaps 30 per cent. of the cases considerable swelling and more or less constitutional disturbance, with a rise of from one to nine degrees of temperature as a rule. Within twenty-four hours, and always within seventy-two hours, all disturbance is over. No other deleterious results have occurred among the many thousands Park has injected. Children of ages between the periods mentioned vary in the amount of reaction according to their age. The youngest children show the least, and the oldest the most, disturbance. A preparation properly prepared and tested is absolutely safe for all periods. As time passes it becomes slightly over-neutralized and loses slightly in its effectiveness.

As to the immunizing results obtained, Park concludes that a few do not become fully immune before the end of the sixth month. Each injection adds to the stimulus and to the accumulation of antitoxin. The response in 500 children of an age between five and ten years who were carefully observed gave the following results:

| No. of Doses of 1 c.c. Toxin- Antitoxin | Number of Children | No. of Children Immune 3 Mos. After Injection | Per Cent. Immune After 3 Months |
|---|-----------------------|---|---------------------------------------|
| 1 | 239 | 175 | 73 |
| 2 | 89 | 80 | 90 |
| 3 | 201 | 191 | 95 |

It is interesting that some 2,400 infants of an age under one week have been injected with absolutely no bad effect. This certainly proves the safety of the preparation.

His observations cover a period of nearly five years, and up to the present time the immunity has persisted in more than 98 per cent. of the cases who developed antitoxic immunity. It seems as if the stimulus of the injections had possibly aroused dormant cell activities to produce antitoxin and that this production having once started continued without further specific impulse.

As to the use of the Schick reaction to indicate the necessity for and the performance of antitoxin immunity, he concludes that when the Schick test is properly carried out it is extremely dependable. If at different times different strengths of toxin are used the results will necessarily vary. The apparent change of negative Schick reactions to positive Schick reactions in children over 2 years of age is explained largely, if not wholly, by the toxin utilized and the technique employed. Drs. Zingher and Schroeder who have done the tests in institutions year after year, have not found a variation, from year to year, of over 4 per cent. Whether even this 4 per cent. represents a real fluctuation in the amount of antitoxin in children, or rather a slight variation in the strength of the toxin used, is uncertain.

They have never observed a case of undoubted clinical diphtheria in a child who had given a negative reaction in a test carried out by a qualified person. There have been a few cases of suspected tonsillar diphtheria with positive cultures. Most of these patients recovered without antitoxin and they, in no way, differed from similar cases in which no diphtheria bacilli were present. It seems correct to regard them as carriers of diphtheria bacilli who developed tonsillitis from other microorganisms

Eradication of Diphtheria by Means of Toxin-Antitoxin Following Schick Testing. E. L. Bauer⁹ in discussing this subject, says that it is generally accepted that $\frac{1}{30}$ of a unit of antitoxin to each cubic centimeter of blood will protect against diphtheria; $\frac{1}{10}$ of a unit

(9) Penn. Med. Jour., April, 1921.

certainly will. The Schick test, when performed by the technique of Park, does show, when negative, that the individual has at least $\frac{1}{10}$ of a unit of antitoxin in his blood, and is therefore immune. If the reaction is positive, then the individual is regarded as susceptible, not having enough anti-toxin to immunize him. The simultaneous performance of the Schick and Römer's tests shows a consistently positive Schick reaction in all who lack $\frac{1}{10}$ of a unit of antitoxin in their blood, and a negative Schick test will be recorded when there is more than $\frac{1}{10}$ of a unit in the blood.

Recently Bauer reported before the Philadelphia Pediatric Society 3,160 tests, and made the following observations:

For all ages he found 1,060 susceptibles and 2,100 non-susceptibles, or 31.8 per cent. were susceptibles giving positive reactions; the highest percentage of positives was 72.5 per cent., occurring in children from 6 months to 3 years; the percentage of susceptibles steadily decreases until but 13.5 per cent. of adults tested were found to be positive.

It was noted that entire families were either positive or negative, exceptions being met with only in the case of adults who might be negative while the children were positive, or a negative found in a very young infant, passively immunized by its mother, while the other children were positive. Subsequently 1,000 more tests were performed and these children showed the same approximate percentages for their ages and consistently showed the same features recorded in the findings of the first 3,160.

In more than 1,200 patients given toxin-antitoxin, including all ages, several facts of interest were noted. In institutions where diphtheria was previously constant and this combined procedure employed, diphtheria does not now occur. Bauer noted that young children give no constitutional reaction to toxin-antitoxin. The older the individual the more apt is a reaction to occur. This is due to the bacillus proteins contained in the mixture, and the reaction is more likely to occur in a person who has a pseudo-reaction as well as a positive re-

action to the Schick test. At least 34 per cent. of adults will give these pseudo-reactions.

Children who react to toxin-antitoxin do so only after the first dose, as a general rule, and reactions to subsequent doses are milder, if they occur at all. The statistics compiled as a result of the work at Girard College, Philadelphia, are significant. Of a total of 1,600 boys 544 received toxin-antitoxin; 119 gave a reaction after the first dose; of these, nineteen reacted after the second dose, but more mildly, and after the third dose nine of the nineteen gave even milder reactions. None who did not give reactions to the first dose gave any reactions to subsequent ones. These boys ranged from 6 to 16 years of age, and as Dr. F. L. Greenwalt, physician in charge at the college, expressed it: "None of the reactions was so severe as many that one sees following vaccination against smallpox."

Considering the low percentage of adults that are susceptible he is of the opinion that these can be ignored with the exception of those whose duties constantly expose them to diphtheria and who might be an economic burden if taken sick as a result of the exposure. Needless to say, he refers to doctors and nurses. The advantage of Schick testing all probationers in training schools will at least aid us in separating the immunes and non-immunes, and advising any susceptible individual who plans to do contagious work to become actively immunized.

Value of the Schick Reaction. Following a comprehensive study of the Schick reaction, Gladys Ward¹ concludes that the Schick test gives very definite data as to which years are the most dangerous with regard to diphtheria infection in a child's life. These are between 6 months and 6 years while the periods of lowest susceptibility appear to be under 6 months and over 15 years. These results are endorsed by clinical experience.

It is of great value in deciding the difficult question of whether a patient is a carrier or is really suffering from diphtheria. For example, a case of streptococcus tonsillitis in a diphtheria carrier would, by culture alone, be thought to be one of diphtheria. If a Schick

(1) Boston Med. Jour., June 25, 1921.

test were done on such a case no doubt would be left—in the case of the test being negative the individual would be treated as a carrier, and if the reaction were positive, as a case of diphtheria. Similarly, in a case with a purulent nasal discharge the same difficulty would arise and a Schick reaction here, too, would indicate the line of treatment to be followed.

It has, perhaps, its greatest value in showing us to whom, among persons exposed to infection (for example, contacts, doctors and nurses) we may safely omit to give antitoxin—thus greatly minimizing the risk of anaphylaxis and also saving pain and expense. When possible only those nurses who give a negative Schick reaction should be employed in diphtheria wards.

We are able by means of the Schick test to ascertain in cases which have previously had the disease or have had antitoxin, to what extent their immunity persists, and whether they have sufficient antibodies to overcome a fresh infection.

Lastly, it has supplied us with a basis on which to build new immunizing methods, which have given such encouraging results in America that we feel justified in looking forward with confidence to the day when diphtheria will be a disease well under control, and the infant and child life of this country robbed of one of its chief horrors.

Experiences with Schick Test. In their experiences with the Schick reaction, A. T. Glenny and R. A. O'Brien² found that there is an error in "filling" capillary tubes with toxin, as described by Zingher last year. They are of the opinion that the clinician is liable to introduce an error in dilutions owing to the difficulty of getting the whole of a minute drop of toxin, which is about 0.02 c.cm., into the diluting fluid. Earlier in their work a batch of toxin diluted in the laboratory sometimes failed to pass their guinea-pig test. It is evident that the conditions must be very rigidly controlled, or the dilution of toxin will not be of standard strength. A serious mistake might arise if practitioners used weak toxin, and, because of erroneous reactions,

(2) Lancet, June 11, 1921.

concluded that certain patients were immune and might be safely left exposed to infection.

Glenny and O'Brien, therefore, make a toxin dilution each week and test it intracutaneously on normal guinea-pigs. They find *m. r. d. i. e.*, the minimal dose that will produce a reaction when given alone—and also the dose that, when mixed with varying quantities of antitoxin, will give a reaction. Their current toxin dilution ready for the Schick test, when further diluted twenty times, causes a reaction in the guinea-pig's skin; 0.1 c.cm. when mixed with 0.0004 of a unit of antitoxin and injected intradermically, must also produce a definite reaction.

As to the stability of diluted toxin, the details of tests presented show that the diluted toxin when kept at 0°C. undergoes practically no deterioration in four weeks, whereas after seven weeks a loss of about 3°0 per cent. in value is found. After seven days at 15°C. the loss in potency is just detectible, while after fourteen days the loss is about 30 per cent. When kept at 37°C. the dilution deteriorated seriously in one day.

These authors conclude that the Schick test is roughly quantitative. A positive reaction does not indicate the total absence of immunity. The test does not divide the population into black and white, but rather into those darker or lighter than a certain shade of grey. If Schick had originally determined on 0.002 of an *m. l. d.* instead of 0.02, it is practically certain that numbers of people who give a positive response to the present standard Schick would give a negative reaction with the weaker dilutions, and would be considered immune to diphtheria. Roughly speaking, people with at least $\frac{1}{30}$ of a unit of antitoxin per cubic centimeter of blood give a negative reaction, while those with less than $\frac{1}{30}$, or with no antitoxin at all, give a positive reaction. As the result of clinical experience Schick decided that it was safe to assume that people with $\frac{1}{30}$ of a unit were immune to clinical diphtheria.

Park and Zingher³ of the New York Health Department, have tested over 52,000 children for the Schick reaction in forty-four schools of Manhattan and Bronx

(3) Med. Officer, Aug. 20, 1921.

during the late winter and spring of 1921. Some of their conclusions in regard to Schick testing and active immunization which these many tests have disclosed are as follows:

1. Children from the home of the well-to-do have a higher percentage of positive Schick reactions than the children of poorer groups of the population living in closely crowded neighborhoods.

2. "Contact immunity" seems to be an important element in the establishment of so-called "natural immunity." Repeated exposure to the diphtheria bacillus in the congested districts seems to cause not only actual clinical cases of diphtheria, but also may produce mild infections of the mucous membranes which are not recognized as diphtheritic, but which may lead to the gradual development of antitoxic immunity.

3. There seems to be a racial factor in immunity to diphtheria. Negro children living in crowded neighborhoods show a high proportion of positive Schick reactions. Children of Italian extraction, living in the crowded East Harlem section, gave the lowest percentage of positive reactions. Jewish children, also living in congested sections of the city, showed a low and children living in the less crowded areas a high percentage of positive reactions.

4. There seems to be a "family factor." There was a marked tendency for all the children of a given family to show the same Schick reaction. Where exceptions to this rule were found, the younger children usually gave a positive and the older children a negative reaction. Again, different families living under closely parallel conditions would often show entirely different Schick reactions. With regard to the capacity for anti-toxin production, there is probably a hereditary tendency on the part of the children of a family to respond either readily, or slowly and poorly, to repeated mild infections with the diphtheria bacillus.

5. Children once reacting negatively to the Schick test continue their immunity for considerable periods of time.

6. Natural antitoxin immunity in human beings, therefore, can be interpreted as due to a combination of

factors in which contact immunization seems to play the most important part. The racial and hereditary factors, however, must also be considered.

7. Schick-positive children who have received toxin-antitoxin treatment should not be certified as immunes until a re-test has been made.

The *Medical Officer*,⁴ commenting on the experiences of Park and Zingher, says that their work appears to indicate that, for the present at least, it will be a better procedure to continue to give the Schick test in conjunction with the prophylactic treatment rather than to give the prophylactic treatment alone, as has been done in some cities. Otherwise large numbers of children, especially the "combined" reactors, will show severe reactions and, in this way, the good-will of the parents, of family physicians and of the children themselves may be lost.

Use of Schick Test and Toxin-Antitoxin in an Institution Population.

Dr. C. A. Earle⁵ has had charge of the children in a large orphanage for more than ten years. In this institution there is always a population of more than 1100 boys and girls between 4 and 15 years of age. Each year some cases of diphtheria have occurred in this group and in some years epidemics of this disease have proven difficult of control.

In 1917, there were eighty-nine cases with seven deaths. In January, 1918, the policy of vaccinating all pupils against diphtheria with T-A. was inaugurated. The proportion vaccinated has increased until now practically all students proven susceptible to diphtheria by the Schick test are made immune by vaccination with T-A.

Since this policy was begun—at first imperfectly carried out in 1918—there have been only twenty cases of sore throat in which diphtheria bacilli were found in the throat. None of the cases was very virulent. There have been no deaths. No intubations or tracheotomies have been done. Eight of these cases developed before T-A. was given, eight at the time or within three

(4) June 20, 1921.

(5) Paper read April, 1921, before Chicago Soc. Int. Medicine.

months of receiving T-A., and four more than five months after its use. One case developed in a child repeatedly found Schick negative.

Of 1164 children examined by the Schick test 35.33 per cent. were found positive. The age distributions of these were 4-5 years, 50 per cent., 6-7 years, 38 per cent.; 8-9 years, 34 per cent.; 10-11 years, 33 per cent., 12-15 years, 28 per cent., over 15 years, 36 per cent.

Contrary to an opinion sometimes stated, Earle not infrequently found one or more Schick-negative children in families where the other members were Schick-positive. Examples—Y. family, children, 13, 8 and 6 positive, child 11 negative. E. family, children 12, 7, 5 and 3 positives, child 10 negative. T. family, children 7 and 5 positives, children 12 and 10 negatives.

As to the efficacy of T-A. vaccination in Schick-positive children, Earle reports that in 274, 87.5 per cent. were negative after 3 T-A.'s. 97 per cent. after 6 T-A.'s, and 99 per cent. after 9 T-A.'s. In 615 children giving each from two to six negative Schicks, three were found to change to positive. The one who developed a diphtheritic sore throat should be added to this list. Earle quotes Theobald Smith in explanation of the fact that in some cases T-A. confers a better immunity than does an attack of diphtheria.

Diphtheria Carriers. G. H. Weaver⁶ in a study of diphtheria carriers among 500 consecutive cases of diphtheria treated at the Durand Hospital, exclusive of laryngeal cases, and those patients who died early, found that after the first week approximately half of the cases that began any week as positive became negative during the following seven days. Three weeks after the onset, 71.2 per cent. of the cases had become negative. At the end of four weeks, 83.2 per cent. were free of bacilli, and after seven weeks, less than 1 per cent, yielded positive cultures. In only a single instance were cultures positive after eleven weeks. The cases are considered as having been negative on the day when the first of three successive negative cultures was secured. If more than one day intervened between the last positive and the first

(6) Jour. Amer. Med. Ass'n., March 26, 1921.

of three negative cultures, the day of the first negative culture has been placed midway between the two.

After an analysis of a series of carriers observed, Weaver concludes that, as is the case with many bacteria, the largest factor in the removal of diphtheria bacilli from the body appears to be destruction by leukocytes. An essential factor in this process of phagocytosis is suitable opsonin.

Efforts at the hospital to clean up carriers are now confined to such measures as aid in removing local conditions that favor the retention of the bacilli. Washes are employed to remove secretions and discharges. Measures are used to facilitate drainage from the accessory sinuses and the nostrils. Irritating solutions are especially avoided. When the bacilli persist after such treatment, operative procedures are instituted if the localization of the bacilli is such that any benefit can be expected. The operations performed have been tonsillectomy and, when the adenoids are enlarged, adenoidectomy. Early disappearance of the bacilli has followed the operations in every case.

Removal of the tonsils and adenoids is advised at the end of a month if the bacilli persist, or as soon afterward as the general condition of the patient warrants. In small children, in whom prolonged isolation is not very objectionable and in whom operative measures are less satisfactory, Weaver is accustomed to wait for the natural disappearance of the bacilli, making use of such local measures as seem indicated. When the bacilli persist in the nose, local lesions in the nostrils, and in children foreign bodies, are looked for.

When an individual has become a carrier, the measures to be instituted should vary according as the bacilli are or are not virulent. In all non-contact carriers the virulence of the bacilli should be tested. This allows most such individuals to be dismissed as not dangerous to others. "Convalescent" and "contact" carriers must always be considered sources of danger. If the carriage is persistent, a test of virulence will occasionally reveal a non-virulent bacillus and allow the possessor to be released from restraint.

Persistent carriers of virulent bacilli generally present

some local pathologic condition in the throat or nose, the correction of which is usually followed by disappearance of the bacilli. No satisfactory means has been devised for destroying the bacilli. When local measures are of value it is usually because they aid in correcting abnormal conditions which interfere with the destruction of the bacilli by the natural bactericidal processes of the body. If such local treatment has been unsuccessful, removal of the tonsils and adenoids will usually be followed by the disappearance of the bacilli.

F. C. Linton,⁷ in discussing diphtheria carriers and their treatment, divides carriers of diphtheria infection into two main categories, *viz*:

Class A. Those in whom no history of a prior attack of diphtheria is obtainable.

Class B. Those who have suffered, or are suffering from, an attack of diphtheria—generally in a site other than the fauces.

Under Class A, he considers those carriers who in practice are usually discovered either (1) in taking specimens from contacts with a case of diphtheria, or (2) in the course of medical inspections of school children, when cases belonging to category "B" are suspected, and specimens taken.

Under Class B, he classes those who have or have recently had diphtheria, usually in a site other than the fauces: He divides this group into the following subclasses.

1. Carriers of nasal type: These are the most frequently discovered source of spread of infection. He found children with the typically inflamed contracted nostril—usually crusted and sore and with a history of bleeding—either in the home or in school class, in following up a case of diphtheria.

2. A discharging ear, in which the K. L. bacillus is lodged, is another source of infection.

3. Wound diphtheria.

4. Animal carriers. Of these the cat has long been reputed to be a possible diphtheria carrier. Savage has performed experiments which go to prove that kittens can not carry the K. L. bacillus. Simons, however,

(7) Med. Officer, Aug. 27, 1921.

records a definite instance of an elderly lady who developed a fatal attack of faucial diphtheria after fondling a cat which had been ill for one week before her illness began.

In regard to the treatment of the persistent carrier, Linton confesses that so far he has not met with any form of treatment that has been an unqualified success. Various remedies—so numerous as to indicate their relative inefficiency—have been tried locally, and he has known intercurrent microbial infections, such as influenzal colds, to clear up all but the most persistent carriers; but the most persistent have resisted all these things. Vaccine treatment is perhaps more promising.

C. G. Guthrie J. Gelien and W. L. Moss,⁸ in a second communication on "Studies of Diphtheria Bacillus Carriers at the Medical Clinic, Johns Hopkins Hospital," conclude:

First: The diphtheria bacilli present in a majority of healthy carriers are avirulent.

Second: Avirulent bacilli can not produce diphtheria.

Third: We have no proof that avirulent diphtheria bacilli can acquire virulence.

For the above reasons they conclude that the carriers of avirulent diphtheria bacilli do not constitute a menace to anyone in particular or to the community as a whole, and that any interference with their liberties on the grounds of their being carriers is unwarranted and unjustifiable.

This stand, of course, immediately raises the question as to what constitutes a valid test of virulence. The authors believe that the standard guinea-pig test may be taken as a safe index of the virulence or non-virulence of diphtheria bacilli for human beings. They have a certain amount of evidence in support of this belief to be presented in a subsequent paper. It may be justifiable, and under certain conditions advisable, to isolate carriers until the virulence of the organism present can be determined, but if the culture proves avirulent for the guinea-pig, further detention of the carrier does not seem justifiable.

They realize fully the time and expense entailed in

(8) Bull. Johns Hopkins Hosp., November, 1920.

applying the guinea-pig test, but think this does not equal the inconvenience to the individual and economic loss incurred by needless isolation of a carrier of avirulent bacilli. There is urgent need of a simpler, quicker and less expensive virulent test.

Fourth: The carrier of virulent diphtheria bacilli occupies quite a different position from that of the carrier of avirulent bacilli. While they think that the danger from the former has perhaps been over-estimated, they recognize the fact that diphtheria bacilli derived from him may give rise to the disease in susceptible persons. In this connection they have pointed out in a previous communication the need of a satisfactory and efficient means of ridding carriers of virulent diphtheria bacilli.

W. L. Moss, C. G. Guthrie and J. Gelien,⁹ reporting on a study of diphtheria carriers in an orphan asylum, conclude:

First: The carrier of avirulent diphtheria bacilli is not a menace to the community.

Second: A positive throat culture, an elevation of temperature and a pathologic throat condition without definite membrane formation are insufficient evidence on which to base a diagnosis of diphtheria with entire certainty.

Third: Virulence tests are necessary to avoid inflicting needless hardships on carriers of avirulent diphtheria bacilli.

A. M. Hewat,¹ in discussing "Problems Regarding Diphtheria Carriers," sets down the following proposals for guidance in dealing with such cases:

1. Swabbing of contacts should be limited to cases in which one has reasonable grounds to suspect a local focus of infection, for example, where there have been two or three or more cases connected with a certain school. He has seen a school outbreak cleared up almost at once by the finding of a carrier. It is wise to swab all child contacts from an infected house before allowing them to return to school.

2. One is not justified in reporting a carrier as a case of diphtheria. He is not suffering from the disease

(9) Bull. Johns Hopkins Hosp., April, 1921.

(1) Med. Officer, Jan. 15, 1921.

diphtheria. As well notify as pneumonia every person harboring the pneumococcus.

3. The isolation and treatment of carriers should only be carried out when

- (a) The organisms have proved definitely virulent to guinea-pigs; or:
- (b) Where other circumstantial evidence corroborates clearly the bacteriologic findings.

Treatment of Diphtheria Carriers with Detoxicated Klebs-Löffler Vaccine. This subject is reported on by A. R. Fraser and A. G. B. Duncan.² They urge the differentiation between the "positive throat" and the true diphtheria carrier. In the former, the bacilli may disappear spontaneously and with energetic treatment will clear up within a reasonable period. The throat which will not clear up, however, and in which the diphtheria bacilli persist with unabated virulence in spite of the most energetic measures of disinfection, constitutes the true carrier.

The grounds on which the authors base their reasons for the use of detoxicated vaccine are that a carrier possesses a certain amount of immunity, and that a rise of his immunity curve to a considerable degree is necessary before his antibody armament can deal successfully with the organisms which he harbors. His immunity would seem to be usually sufficient to inhibit the organisms, but quite insufficient to exterminate them; in other words there is a balance of power.

From a close study of the three cases studied in detail, they conclude that in the use of detoxicated vaccine we have a method of promising efficiency in dealing with contacts, convalescents, and carriers. Antitoxin protects only from the toxin produced by the living Klebs-Löffler bacilli in the tissues. The vaccine prevents the growth and life of the bacilli. In a case of diphtheria both vaccine and antitoxin should be given. The advantages of dosage allowed by employing detoxicated vaccine must not be overlooked.

The dose which they found most effective and yet harmless was 4,000 million initial dose, 120,000 million at end of a month, and 350,000 million at the end of

(2) *Lancet*, Nov. 13, 1920.

approximately two months, running the dose up gradually in the intervening intervals.

Diphtheria Control. B. W. Carey,³ in discussing the control of diphtheria, considers that the main factors which may be held responsible for the continued undue incidence and high mortality are three:

First, and the most important, the incomplete application of procedures of proved worth for the prevention and control of diphtheria, for in the hands of public health workers has been placed a complete armamentarium with which to wage our fight.

Second, the failure of early diagnosis, and the tardy and often insufficient use of antitoxin.

Third, the lack of realization by parents of the seriousness of the sore throats of childhood and adolescence, with the resulting delay in securing proper medical attention.

As to the percentage of recurrences, he states that it must be admitted that 25 per cent. of the undue incidence of diphtheria in Massachusetts for the past year has been recurrences in the same communities. One of the larger cities of the commonwealth reported, for a period of eighteen months, nearly 500 cases, 32 per cent. of which furnished evidence of multiple household or neighborhood infection. Ninety of these multiple cases indicated a probable exposure to a common source of infection, being reported within forty-eight hours and from thirty-nine households. Seventy-three cases from thirty-seven households were reported four or more days later than the initial case in the household, and fifty-one cases in forty-four families gave a history of contact with a case in an adjoining or nearby house.

He believes that if proper and adequate measures were taken promptly on the discovery of the initial case, the number of secondary infections might be greatly reduced, but the *sine qua non* of the control of diphtheria is found in the use of the Schick test, with the immunization by toxin-antitoxin of those who do not possess a natural immunity.

As general remedies to lessen the incidence and mortality of diphtheria, the following are especially emphasized:

(3) Jour. Amer. Med. Ass'n., Aug. 27, 1921.

Education of physicians and the laity to the fact that all agencies are available for the immunization of the susceptible, and for the diagnosis and the treatment of the disease.

Intelligent study and treatment of the "carrier" or perhaps more correctly, the "missed case."

Education of the laity to the fact that diphtheria is often insidious in onset and mild in course, and recovery is uneventful for the patient, yet serves as the focus of multiple infections of a far more virulent type.

Education of local health officers as to the necessity of intensive investigation of the source of each case, and of the necessity of immunizing other members of the infected household.

Essential Preventive Measures. G. H. Weaver⁴ lays down some essential points in the prevention of diphtheria, based on a study of 147 fatal cases. He is of the opinion that assumed results have not been realized, and that there has been little appreciable improvement in recent years in dealing with this disease.

The fatality rate in diphtheria in Chicago from 1912 to 1919 is given in Table I. While there is a slight fluctuation from year to year, it is evident that there has been no appreciable decrease in the proportion of cases of diphtheria in which the patients die. The fatality rate for the last four years is almost the same as that for the preceding four. The figures justify the conclusion that in Chicago advantage is not being taken of the means at hand for the cure of diphtheria.

TABLE I. FATALITY RATE OF DIPHTHERIA IN CHICAGO

| Year | Per Cent. | | Year | Per Cent. | |
|---------|-----------|-------------------|---------|-----------|-------------------|
| 1912... | 13.04 | } 11.63 per cent. | 1916... | 11.26 | } 11.31 per cent. |
| 1913... | 11.08 | | 1917... | 11.82 | |
| 1914... | 10.87 | | 1918... | 12.67 | |
| 1915... | 11.60 | | 1919... | 9.31 | |

In 147 fatal cases in his series, eighty, or 54.4 per cent. of the patients, received no antitoxin at home, and nine of them died almost at once after admission to the hospital, six before any antitoxin could be given.

Of these patients, 70.2 per cent. received their first antitoxin between the third and sixth days. In all the

(4) Jour. Amer. Med. Ass'n., June 11, 1921.

cases in which the first antitoxin was given on the first day, the dose was small and the disease progressed in spite of it. In no single case had an adequate amount of serum been given early.

Of the seventy-five deaths investigated by the Chicago Department of Health, twenty-seven are put down as due to failure of physicians to make an early diagnosis, and twelve as probably due to insufficient antitoxin.

Weaver concludes that the defects in the management of diphtheria among physicians may depend on the following causes:

1. Failure to make cultures from sore throats.
2. Failure to administer antitoxin at once and in every case which looks suspiciously like diphtheria, without waiting for the result of cultures, or in the presence of a single negative culture.
3. Failure to follow patients with sore throat after seeing them once.
4. Insufficient doses of antitoxin, which were often given, especially in toxic cases. In diphtheria a therapeutic dose of antitoxin should be at least 5,000 units, and often from 10,000 to 20,000 units.
5. Failure to get the antitoxin quickly in contact with the circulating toxin. Almost without exception the antitoxin given patients at their homes has been injected subcutaneously, although much prompter effects follow intramuscular injection.

So much has been said and written about anaphylactic shock from serum that an unfounded fear of this accident seems quite widely spread among physicians. Anaphylactic shock from serum is a very rare occurrence. Compared with the danger from diphtheria, its danger is infinitesimal and is to be ignored.

Comparative Studies of Diphtheria Cultures and Swabs. For many years it has been the practice of state and city boards of health to send out Loeffler's culture media for the collection of material for the diagnosis of diphtheria. It has been considered bad practice to ship the original swabs to a laboratory for diagnosis. We have always supposed that desiccation and the lack of food greatly reduced the viability of the Klebs-Loeffler bacillus.

C. C. Young and Minna Crooks,⁵ in studying this question in the laboratories of the Michigan Department of Health, came to the conclusion that:

The diagnostic value of swabs and culture media is equal.

The swab has additional diagnostic value for other infections, notably septic sore throat and Vincent's angina.

The swab reduces the dangers of contaminated cultures one-half, for inoculations are made under more favorable conditions in the laboratory.

And last, but not least, the cost of the swabs is very much less than tubes of culture media.

Degree of Immunity Insured by Negative Schick Test. A negative Schick test in cases which have an active immunity, either natural or acquired, when the toxin used and the technique employed has been suitable, W. H. Parks⁶ says, shows an almost complete security from diphtheria, not only immediately, but for the future.

He reports that immune persons may harbor diphtheria bacilli and that with an intercurrent tonsillitis these germs may be found in the cultures. In an outbreak studied by him the fact that an extraordinarily large percentage of all the children in the institution were carriers of virulent bacilli, and only one group developed cases of tonsillitis with pseudo-membranous patches, makes it uncertain that the cases were diphtheria.

Diphtheria in Immunized Children. S. A. Blauner⁷ finds that diphtheria can occur in children who possess either natural immunity or are immunized by the toxin-antitoxin method.

An experience in a carefully supervised orphan asylum has shown that diphtheria in epidemic form can occur among immunized children, and that the value of a negative Schick reaction is not universal. The author does not present any figures or analysis of these outbreaks, or observed cases, therefore his findings must be

(5) Amer. Jour. Pub. Health, March, 1921.

(6) Amer. Jour. Dis. Child., July, 1921.

(7) Ibid., May, 1921.

taken with some reserve, in view of all the other favorable evidence.

Milk-Borne Outbreak from Infected Finger. J. E. Henry⁸ reports an outbreak of diphtheria in Williamstown, Mass., traced to a dairy farm on which was found a girl with a sore right index finger. The girl had worked in the dairy all the time, either milking, delivering milk or helping in other ways.

The nail was gone on the finger and the sore was covered by a soft, brownish scab, which on removal showed a whitish exudate. Cultures from this showed *B. diphtheriae*.

The dates of onset of thirty-two cases traced directly to the milk were: August 12, two; August 14, two; August 16, three; August 17, one; August 18, nine; August 19, five; August 20, two; August 21, one; August 22, one; August 23, three; August 24, three.

No further cases occurred until September 15, at which time there was a second outbreak of fourteen cases, with onsets September 15, 18 and 19. The infected milker had returned home and gone to work, September 11. It was discovered that one of the cows had a teat infected with *B. diphtheriae* and also that the owner (a milker also) had the infection in a sore on his hand. He stated that he mashed his hand with a hammer on September 13.

SCARLET FEVER

Desquamation in Scarlet Fever. The *Medical Officer*,⁹ in discussing this question editorially, says that the growing opinion of the medical profession that in the later stages of scarlet fever the desquamated skin, especially on the soles of the feet and the palms of the hands, has little or nothing to do with the spread of infection has not infrequently given rise to rather difficult positions. There are good clinical grounds for believing that the throat is the primary site of infection and hence it is reasonable to suppose that all exudate from that part of the body, whether discharged through the mouth, nose,

(8) Jour. Amer. Med. Ass'n., Dec. 18, 1920.

(9) Nov. 20, 1920.

or by way of the Eustachian tube from a running ear, is virulent and capable of conveying the disease to a susceptible person. The virus of the disease, whatever it may be, is certainly present in the blood, and the characteristic rash may be taken as good evidence that the skin is performing its function as an excretory organ in common with the kidneys, the congested condition of the capillary blood-vessels in both forming at least a suggestive analogy. There is therefore nothing inherently absurd in the supposition that the desquamated skin is, or can be infectious, but it is not so easy to believe that that infection can still be active in the hard skin of the palms and soles after the repeated soaking, rubbing and scraping with disinfectants and other applications that are usually practiced in hospital in order to get the patient fit for discharge.

The failure of inunction treatment to effect any decided modification of the incidence of scarlet fever, combined with the considerations mentioned, have led many to suppose that the skin plays a very minor part in spreading the disease, and on that account it has become the custom at many isolation hospitals to discharge a patient after four or five weeks, although desquamation on the remoter parts of the body is incomplete, provided the general health is good and there are no remaining signs of inflammation or morbid discharge from the throat, nose or ears.

As a matter of experience, the period of from six to eight weeks which elapses before desquamation is complete usually covers the time in which most of the complications of scarlet fever occur, and is well beyond the average time taken to clear the throat of diphtheritic infection. It is quite likely that, as a rule, scarlet fever infection dies out in the same time, but such an arbitrary rule is not in consonance with modern scientific methods and the time seems opportune for some definite pronouncement to be made by an authoritative body as to what points should be considered in determining the cessation of infection.

Scarlet Fever Quarantine. W. B. Braley¹ of Highland Park, Michigan, recounts two years' experience with

(1) Jour. Mich. State Med. Soc., September, 1921.

the 21-day period of quarantine in scarlet fever. Unfortunately, the series of cases is comparatively small as one might expect with a city of a population of about 40,000 people.

The rule which he followed was a 21-day minimum quarantine in the uncomplicated cases and one week additional restriction before attending schools or other assemblies. Also, if possible, isolation or removal from the primary case all exposed children and holding them for one week for observation.

Desquamation, in his opinion, is not a means of spreading the disease, but the desquamation when contaminated by the mucous discharge from the ears, nose and throat or broken-down glands, may become an infectious agent.

In endeavoring to arrive at a definite conclusion as to the necessary length of detention in scarlet fever he relies on two points in determining the period:

1. The intensity of the disease. The mucous membranes in the severe cases are affected more severely and the mucous discharge will last longer.

2. Glandular involvement with discharges. This is a factor which should determine a much longer quarantine.

During the four years that the 21-day period of quarantine has been in effect to a "greater or less" extent, the number of cases of scarlet fever have run, as follows:

| Year | Est. Population | No. Cases | Av. Days' Quarant. |
|-----------|-----------------|-----------|--------------------|
| 1917..... | 37,000 | 238 | 23 |
| 1918..... | 38,000 | 80 | 24 |
| 1919..... | 39,000 | 112 | 26 |
| 1920..... | 43,000 | 173 | 23 |

Wm. De Kleine, in a discussion of Braley's paper, said that in the city of Flint the 21-day quarantine was begun in May, 1919. From May, 1919, to May, 1920, there were 282 cases reported, and from May, 1920, to May, 1921, there were 467 cases reported, a total of 749 in the last two years, as compared with about 850 for the two previous years.

Spread of Hemolytic Streptococci. R. Tunncliff² states that hemolytic streptococci may be isolated from

(2) Jour. Infec. Dis., July, 1921.

the floor and walls of rooms occupied by patients suffering from scarlet fever and diphtheria, from the fingernails, shoes and masks of attendants, and from the eating utensils used by the patients.

Only five of the twenty strains isolated were opsonified and agglutinated by the serum of sheep, immunized with a hemolytic streptococcus from scarlet fever, and hence considered as specific for the disease.

The experiments also suggest that while patients with scarlet fever generally rid themselves of specific hemolytic streptococci in from three to four weeks, patients with discharges may retain them longer, and that specific streptococci disappear generally when the scarlet fever patient becomes non-infectious, according to clinical experience.

MEASLES

The Control of Measles. The London County Council in November, 1920, decided to invite the Metropolitan Borough Councils to appoint representatives to attend a conference for the purpose of considering measures for the better control of measles in London. The conference was held at the County Hall on Feb. 25, 1921.

The *Medical Officer's* summarizes the report of the proceedings as follows:

The conference was invited to consider (1) proposals for further legislation, and (2) proposals for making more effective the existing powers of the council and the local sanitary authorities.

No proposal for further legislation in respect of measles was made at the conference. Under heading (2) a resolution was passed, as follows:

That for the better control of measles in the county of London, there should be the fullest measure of co-ordination between the central and local authorities and other agencies concerned in the care of children; and it is desirable that—

1. Every effort should be made through the school organization to obtain the earliest possible information with regard to the reasons for absence from school of children, especially those attending infants' departments, and that the fact

(3) July 9, 1921.

- of the existence of measles in the homes of the children should be communicated at once to the local medical officer of health.
2. Steps should be taken, if possible, to insure that parents and guardians of children liable to attend school should notify the head teacher of the school within forty-eight hours when a child is kept away on account of ill health, stating the apparent nature of the illness or indisposition from which the child is suffering.
 3. Every possible effort should be made to develop the provision of nursing assistance in the case of measles, and that the authorities of all hospitals and dispensaries, and private practitioners, should be made aware of the facilities that exist for obtaining nursing assistance in the case of measles, and that forms should be supplied to them upon which application could be made for nursing treatment in suitable cases.

In reference to existing arrangements it was noted that the knowledge of measles cases is obtained to a great extent through the attendance of children at school, and the control of the disease is necessarily dependent largely on the utilization of the resources of the school organization and the school medical service. In criticism of the arrangements, it was urged by representatives at the conference that under the arrangements normally obtaining there is considerable delay in the detection of cases of measles through the school organization, and consequent delay in communicating to the borough medical officers information as to cases so detected.

In order to meet the proposal in the resolution of the conference, the education committee are prepared to take steps to secure the issue to school teachers and attendance officers of a general instruction enjoining them to acquaint the borough medical officers at once, on forms already used for reporting cases of infectious illness, of all detected cases of measles, with information of any special circumstances within their knowledge, particularly where young children under school age are affected and where home conditions are unsatisfactory.

The conference also proposed that steps should be taken, if possible, to ensure notification by parents and guardians of absences due to illness and the apparent nature thereof.

It should be noted that these measures were apparently deemed necessary because measles in England and Wales is not a reportable disease.

In 1915, measles was made compulsorily notifiable throughout England and Wales by an Order issued by the late Local Government Board, and in 1919—after four years' operation—the order was rescinded by the Ministry of Health, as the result of consideration of various criticisms as to the ineffectiveness of the order. In communicating this decision, the Ministry pointed out that local authorities were free "to organize various forms of combating and preventing the spread of the disease immediately on receiving information respecting cases of measles occurring in their districts from the many different local sources of information now available."

The conference, after a consideration of this question, passed a resolution "that the notification of measles by the medical profession is necessary for the following purposes, *viz*:

1. To secure the prompt segregation of susceptible contacts attending the public elementary schools; and
2. To render efficient any provision of nursing aid by the local authority."

The public health committee of the London County Council, in its report of the conference proceedings, comments on the aforesaid resolution, as follows:

"We concur in the opinion of the county medical officer that the detection and reporting by the school organization of cases of measles gives a more complete result than would be attainable by compulsory notification; and that if the public money needed for compulsory notification were spent on additional nurses or health visitors, or on after-care, there would be—with the existing means of securing information of cases—a far greater prospect of reduction in mortality due to measles and of amelioration of the vast amount of ill-health and physical defect for which measles is largely responsible.

"The resolution of the conference in favor of the compulsory notification of measles by the medical profession was not a unanimous decision, as a considerable

minority voted against the proposal. In our opinion the improved arrangements suggested in this report for detecting cases of measles, and giving the officers of the borough councils the earliest possible notice thereof, will go far towards meeting the objects of the resolution, and should certainly be tried in preference to an immediate extension of compulsory notification throughout London."

WHOOPING COUGH

Vaccine Therapy is the Most Rational and Effective Method of Preventing Whooping Cough in Public Institutions. C. J. Bloom and G. J. De Reyna⁴ report good results from the prophylactic use of vaccine in preventing the spread of whooping cough in an orphan asylum in which five cases of the disease occurred in April, 1919. Practically all the remaining children had been subject to infection, the total number being 204, ranging in age from 10 days to 6 years, ninety-seven being 1 year of age or under. This asylum cares in the main part for the greater number of illegitimate children born in the institution, city, and in neighboring parishes. A large percentage of those admitted are marasmic; others show different manifestations of malnutrition, and many give signs of congenital lues.

The vaccine employed in this institution was a mixed stock vaccine (recently prepared within one month). No preservative was used in the manufacture of the same. Each cubic centimeter of the vaccine contained 5,000,000 Bordet-Gengou bacilli and 3,500,000,000 influenza bacilli.

The dosage was as follows: Infants under 6 months, 0.25 c. c., three doses on alternate days. Infants from 6 months to 1 year, 0.5 c. c., three doses, on alternate days. Children from two to six years, 1.25 c. c., three doses, on alternate days.

In previous years not less than 50 per cent. of the entire number of children living in this institution contracted whooping cough. From the first week in May,

(4) New Orleans Med. and Surg. Jour., April, 1921.

1919, to the first of January, 1920, there was not a new case of whooping cough noted in the institution.

SMALLPOX

The Abolition of Smallpox. This is considered by W. McConnel Wanklyn⁵ in an address before the Annual Meeting of the Association of Public Vaccinators of England and Wales. He said that it was his aim and object to keep smallpox out and that was identical with the aim of all vaccinators. They know the present waste from smallpox and the risk of calamity in the shape of a smallpox epidemic. The true and ultimate objective is to attack smallpox, throw it out of the country and keep it out. Success can never be achieved by merely planning to prevent smallpox.

He urges that smallpox must be regarded as a world disease; as we live in the world we must needs be exposed to it. This factor is one of our main dangers. As often as smallpox was checked in England and Wales inland, even to the point of extinction, it was brought in again from overseas and re-appeared.

To the proper application of vaccination during the war, the almost complete freedom of troops from smallpox could be attributed. He is of the opinion that the whole population could and should be brought into the same position of security.

In concluding, Wanklyn declared from his own personal knowledge of the subject that daily we are near an epidemic of smallpox on a large scale, which once begun hardly anything but the lapse of time could stop. Once begun this would necessitate beyond all shadow of a doubt a huge expenditure, certainly running into millions of pounds. The proper way of prevention is to look the facts in the face.

"Also, we should consider the heavy cost of existing anti-smallpox administration and the immensely greater expenditure which is constantly so near. It would be calamitous, indeed, to life, to efficiency, to business, to finance, and to general health administration if, in

(5) Med. Officer, Feb. 26, 1921.

addition to our existing troubles, there supervened an epidemic of smallpox."

Antagonism to Vaccination. In 1904 it became apparent to W. S. White⁶ that, in reference to vaccination against smallpox, there must be more than ordinary cause for so much criticism and fault-finding and that there was need for investigation to ascertain the reason for the common antagonism of the laity. It did not take long to find that the necessity of vaccination was looked upon by a great many people as imaginary while others who believed in its efficacy were not enthusiastic because they had had unpleasant experiences, such as sore arms or legs which left them the possessors of hideous scars after submitting to that which promised to be a simple operation. There seemed also to be no intelligent understanding as to the length of time immunity could be hoped for, neither was there any uniformity in the technique or methods of the vaccinators. Furthermore, the scars representing successful takes known as typical, were of such varying shapes, sizes and appearance, that confusion of necessity existed in the minds of many physicians and of more patients—a state of affairs very much to be regretted, but which up to the present time has not greatly improved. These conditions and doubts naturally bring up the question, what is to be done to establish the true status of vaccination, eliminating some of the disagreeable features and all of the avoidable happenings?

He concludes that it should be obligatory that each vaccinator should use the best virus obtainable, that of accredited laboratories only; should have it fresh, in hermetically sealed tubes, and keep it in refrigeration according to specified directions. There is nothing used by the medical profession more susceptible to atmospheric conditions, or more perishable than vaccine virus.

In summing up the work on vaccination it is the author's belief that a regular system, similar to that outlined below, will be of advantage to all future work in vaccination:

The cool and cold months should be selected when possible.

(6) Ill. Med. Jour., March, 1921.

Use nothing but fresh virus of accredited laboratories.

Vaccination should be done with all the precautions as to cleanliness that is customary in the case of surgical procedures.

Do not unnecessarily mutilate or destroy the integument.

Three points of inoculation give the best results.

Never dress vaccination wounds, but permit them to get plenty of air.

Record all primary vaccinations with the date, age and results.

Record all re-vaccinations in the same careful manner as the primary.

Study scars of typical vaccination, observing closely the immunity they give the individual.

Records full and complete, from which statistics may be compiled, will ultimately define the protection accorded one typically vaccinated.

Smallpox in England. A note of patient resignation with regard to the smallpox situation in Great Britain comes from the pen of that staunch defender of the public health, Stephen Paget.⁷ The antivaccination movement is too strong and the ravages of smallpox are too mild to warrant hope that the nation will be brought around to a policy of vaccination. Great Britain has ceased to be a well-vaccinated country. As time goes on it will become less so. When smallpox some day gets a start, as some day it will, there will have to be hurried vaccination of millions of people and even then many will die and many thousands will suffer because of the false teachings of the antivaccinationists. The experience through which Glasgow has just gone stops the wave somewhat, just as that of Gloucester in 1895-96 stopped it to a considerable extent but markedly to impede it something much more serious will be required.

So far as the average British subject is concerned, he believes in the efficacy of vaccination. For that matter so does the antivaccinationist. Few take any stock in the wild, malicious lying statements of the propagandists but the average citizen does not think the danger of smallpox great enough to warrant him in incon-

(7) Inter. Jour. Pub. Health, March-April, 1921.

veniencing himself to any serious degree. He thinks the health officer wants to carry out the program because of his faith in its effectiveness, his pride in his work and, in some measure, because the procedure has been called into question. Like every other man he becomes over-imbued with the importance of that which constitutes his life work. Though the average citizen rather honors him for that he, at the same time, distrusts him to the extent that he judges for himself as to how much of the program he will go along with. Vaccination is beginning to be regarded as we regard those doors in theaters which are marked "emergency exit." The majority of Englishmen and Englishwomen are inclined to keep it for that purpose only and to see what will happen.

"The gradual subsidence of the disease and its milder character during the past thirty years, in spite of the lesser number of people vaccinated, has been the greatest factor in the development of this Micawber sentiment. This popular attitude might not have developed had the medical profession forty years ago been more united in the cause of public health. But it's too late to worry about that now. We can only await the oncoming of disaster with resignation and trust to the authorities of that time and place to pull their people out as promptly and with as little loss of life as possible."

Quarantine in Smallpox. In reference to the question whether smallpox may be controlled by quarantine measures, in lieu of vaccination, as is held by some, W. J. Hanna⁸ says that the general laws of the State of California require that each person who has contact with a case of smallpox, subsequent to the appearance of the smallpox eruption, shall be vaccinated or put in quarantine for a period of twelve days. There is no reason why a person who is afflicted with smallpox should be quarantined, except that people who refuse to be vaccinated are protected from the disease. One of the main reasons why antivaccination propaganda is spread, is because conscientious objectors feel safe from contracting the disease on account of rigid quarantine. With these facts before us, he recommends that free vaccination be offered, and quarantine of smallpox be abolished.

(8) Calif. State Jour. of Med., May, 1921.

Control of Smallpox in California. The California law relating to vaccination as a requirement for school attendance has two affirmative features and three which negative the law. The first two provisions require a certificate of the vaccination or of the health officer that a successful vaccination has been done within seven years. The three negating provisions say that such certificate will not be required if a physician certifies that he has tried repeatedly but unsuccessfully to vaccinate the individual, that he is naturally immune to vaccinia or, that the parents or guardians are conscientiously opposed to vaccination.

J. N. Force⁹ says that 80 per cent. of the school population of California is now unvaccinated largely because the last provision offers an easy way out of expense or trouble and the public is no longer afraid of vaccination. The proof that the element of conscientious objection is merely a subterfuge is given in two experiences at Berkeley in which about 95 per cent. of the so-called conscientious objector children were promptly vaccinated by request of parents when there appeared danger immediate enough to be appreciated by the parents or where vaccination was the least troublesome of alternative procedures. Force tells us that the constitutional objector clause of the law has twice been declared unconstitutional by California courts (*William vs. Wheeler*, Appellate Decisions, Vol. 18, page 51; see also same case in superior court).

The result of this large gain in the proportion of the unvaccinated in the California schools is a reversion to the type of age distribution which prevailed in the days before Jenner. In other words smallpox in California has again become a disease of children. California, thanks to this law, has gone back to where Scotland was two hundred years ago. The number of cases of smallpox in California has risen from 91 in 1915 to 2053 in 1919 and 4486 in 1920. Of 4226 of the 1920 cases 92 per cent. were never vaccinated, 7 per cent. were vaccinated more than five years before and 1 per cent. were vaccinated within five years. The curve of age distribu-

(9) Amer. Jour. Pub. Health, February, 1921.

tion showed the maximum number of cases at age 6 in 1916; at age 8 in 1918 and at age 8 in 1919. In each year there was a decrease in the years of adolescence and then a second peak. In 1916 the second peak occurring at age 33 was 75 per cent. as high as the first. In 1918 at age 38 was 60 per cent. of the first and in 1919 the second at age 40 was 40 per cent. as high as the first. The childhood peak of 1918 was three times as high and that of 1919 was eight times as high as that of 1916.

Of 205 patients in 1916 five were over 60 years of age, one was 78. Of 654 cases in 1918 nine patients were over 60 and of 1560 cases in 1918 forty-two were over 60, one was 78.

In the University of California they ignore the fifth provision of the law, the conscientious objector clause declared unconstitutional by the courts. They accept a vaccination scar as reasonably good evidence of immunity to smallpox regardless of the age of the scar. They vaccinate all those without scars and accept all those with scars. This policy has been in operation since 1906 and it has worked. This supersedes three of the four provisions of the law.

Experience proves that there is no such thing as a person naturally immune to vaccinia. If cold fresh potent vaccine is used all persons who have not had vaccinia can be successfully vaccinated. In 300 entrants with no scars but with histories of previous unsuccessful attempts to vaccinate Force, by using fresh cold vaccine, got 297 primary vaccinias.

The only way to determine a person's susceptibility to vaccinia is to vaccinate with fresh cold vaccine and to observe the site for one of three reactions, primary vaccinia, secondary vaccinia or the immune reaction. The possession of a well-defined vaccination scar is not evidence of immunity to vaccinia. Kitasato found that 14 per cent. of persons successfully vaccinated could be successfully revaccinated within a year. Nevertheless the only practical method of controlling smallpox is to examine for scars. All persons not having scars are vaccinated or excluded from school. No certificates of any character are accepted.

PLAGUE

Plague Control. The methods of plague control are summarized by F. Simpson.¹ In California he reports that plague is confined to a small endemic focus among the ground-squirrels. The flea found infesting these animals and their burrows is usually present in great numbers, and the ground-squirrel appears to be its selective host. It readily bites man.

The three plague rats of the United States with which we are concerned, are the Norway, or *Mus norvegicus*; the Alexander rat, or *Mus alexandrinus*, and the Indian black rat, or *Mus rattus*. All are flea-ridden, all are semi-domesticated, and all litter continuously throughout the year. All are homed in our seaports and under normal conditions all will be found occupying the same premises—the Norway in the ground under floors *M. rattus* and *M. alexandrinus* in the walls and on upper floors.

He concludes that if we are economically and efficiently to ward off plague we must rid ourselves of the rat. This demands coördination of effort, management, organization and funds. Rat destruction and rat-proofing are preventive measures that fortunately do not involve financial loss, while they will eliminate the dangerous rodent from the homes and environment of men.

Detection of Rodent Plague. The signs of plague as they occur in rats and guinea-pigs and the laboratory procedure employed in their detection and confirmation are outlined in a paper by C. L. Williams.² He states that upon the demonstration of the presence of plague depends the institution of eradicated measures. If the infection is severe, intensive eradicated measures must be applied as rapidly and completely as possible; if light, time may be safely taken for the organization of a smaller but more efficient and less expensive force, a contrast of conditions recently illustrated in Beaumont and Galveston, Texas. Delineation of the infected area enables the concentration of eradicated efforts within it, though trapping must to some extent be maintained

(1) Amer. Jour. Pub. Health, November, 1920.

(2) Ibid.

in all parts of the community in order to detect at once any spread.

The diagnosis of infected rats is in the last analysis based upon a demonstration of the presence of *Bacillus pestis*, although in actual practice many cases are declared positive after a review of the gross lesions only. However, having confirmed the presence of *B. pestis* in the first rodent case many of the subsequent ones may be safely diagnosed from gross lesions.

The cardinal or major signs of acute plague are five in number: injection, bubo, granular liver, large dark spleen and pleural effusion. It is rare that all occur in any one rat, and equally rare that any of them appears alone. These signs are characteristic of plague, and occur in other conditions with such exceeding rarity that most workers in this field are inclined to agree with the Indian Plague Commission that a well-marked case may be safely diagnosed even when culture and animal test are negative.

As to the proportion of rats infected in a plague-infected territory, Williams states that in this country, where eradication is begun early, the trapped rats brought to the laboratory seldom show more than 2 or 3 per cent. infected, and usually lower.

As eradication proceeds, the proportion of infected rats declines, rapidly at first, then more gradually and may go as low as 0.01 per cent. or less before becoming zero. The highest proportion recorded in this country was recently seen in Beaumont, Texas, where seventy-five or 15 per cent. of the first 500 rats were found infected.

ENCEPHALITIS LETHARGICA

Study of Thirty-nine Cases. W. St. C. McClure³ presents "A Local Survey of Encephalitis Lethargica," based on thirty-two cases occurring in Manchester during 1920. During 1920 and in the early weeks of 1921, thirty-nine persons, in whom the date of onset of illness was in 1920, were reported to be suffering or suspected to be suffering from this disease. After investigation

(3) Lancet, Feb. 19, 1921.

and observation thirty-two were accepted as true cases, some other diagnosis being subsequently arrived at in the other seven.

The disease showed no signs of infectivity—that is to say, no connection was traced between the cases which were widespread over the city, nor did infection spread to any of 138 family contacts. No common source of infection was found. As regards the milk supply, for instance, of the thirty-two persons affected, four habitually consumed condensed milk, and the remainder obtained their milk from twenty-eight different sources. Nor does transference by means of other foods seem likely, though the investigation in this direction is incomplete. Housewives and workers were attacked in about equal numbers, scholars and infants did not escape. It is certain that cases of encephalitic lethargica occur which remain unrecognized and escape investigation, and so connecting links may be missed. Nevertheless, the conclusion may be deduced either that the disease is not infectious or that the infective material is widespread, and that there exists among the majority of people a natural immunity to it.

It is McClure's opinion that until our knowledge becomes more complete encephalitis lethargica should be presumed to be infectious or contagious and precautions taken accordingly.

The *Medical Officer*⁴ commenting editorially on encephalitis lethargica says:

Dr. F. G. Crookshank in 1919 published a paper in the Proceedings of the Royal Society of Medicine (Vol. XII), in which he worked out, learnedly and with care, the history of epidemic encephalomyelitis. His historical researches showed that clinical conditions which we now call by various names (such as polio-encephalomyelitis, polyneuritis and encephalitis lethargica) have been recorded by the medical faculty and others during the last 450 years at least; and that for the most part these occurrences have been noted as incidental to the sweating sicknesses, influenzas and catarrhs.

Rôle of Filtrable Virus. W. Thalheimer⁵ presents

(4) March 5, 1921.

(5) Archiv. Neurol. and Psychiat., February, 1921.

evidence confirming the results of Loewe and Strauss with respect to the filtrability of the virus from cases of encephalitis lethargica.

From four cases, two of the fulminating type, he obtained a minute filtrable microorganism, which he successfully cultivated in ascitic fluid tissue medium, from brain substance and spinal cord fluid. He believes that this organism is identical with the one described by Loewe and Strauss.

TYPHOID FEVER

Preventive Measures in British Army. In the Finlayson Memorial Lecture, William B. Leishman⁶ reports on "Enteric Fevers in the British Expeditionary Force, 1914-1918." Of preventive measures he speaks especially of inoculation and carriers.

The carrier problem in general, he says, is sufficiently difficult to deal with in times of peace, but in war, although our powers are greater, the difficulties are enormously multiplied, while the grave potentialities consequent upon the presence of undetected germ carriers among troops in crowded and often insanitary surroundings are obvious. In the British Expeditionary Force it was a rule that every diagnosed case of typhoid, paratyphoid or enteric group infection should, when fit for transport, be invalided home, neither the accommodation nor the conditions being altogether suitable in France for the necessary prolonged period of convalescence. Consequently, it fell to the medical authorities at home to carry forward and complete the bacteriologic tests requisite to establish, with reasonable certainty, the eventual freedom of the convalescents from the carrier condition.

To this end, centralization of the returned convalescents was obviously the best means of securing both uniformity of practice and economy of labor. This was arranged for by the creation of typhoid convalescent depots, and eventually a single depot. In these depots, the case was carefully followed up, and the rule observed that no patient should be allowed, under any

(6) Glasgow Med. Jour., February, 1921.

circumstances, to return to an Expeditionary Force until at least three consecutive bacteriologic examinations of the excreta, conducted at intervals of seven days, should have proved negative. Cases in which the chronicity of the carrier condition had already been established, either overseas or at home, were naturally subjected to a still more rigorous standard of cure, in view of the well-known intermittency which such chronic carriers may at times present. These precautions worked excellently, very rarely a healthy carrier was encountered in France. Cases, however, did occur, usually detected as the result of the rigorous investigations undertaken in connection with some small explosion of fever of uncertain nature in a unit. In a number of these a typhoid or a paratyphoid carrier was run to earth, and usually found either to be a man who had had an attack of one of these fevers before the war or who, during the war, usually through some error of diagnosis, had escaped the meshes of the net spread for his capture.

The low typhoid rate in the British Expeditionary Forces Leishman attributes in no small measure to the efficiency with which this organized campaign against the carrier was conducted.

In reference to inoculation, attention is called to the fact that by degrees the number of cases of paratyphoid under treatment in hospitals came to exceed those of typhoid, the lines crossing one another in the month of June, 1915, and from that time till the end of 1918 paratyphoids retained this preponderance. Both forms were represented, but paratyphoid "A" was always rarer than paratyphoid "B," the British experience in this being the reverse of that of their French colleagues.

In view of the general recognition of the protective value of typhoid vaccine, it was natural that similar hopes should be held on the possibilities of protecting against paratyphoid infections, either by a separate vaccine or by one in which paratyphoid bacteria were mixed with typhoid.

Experiments were carried through successfully under the direction of Colonel D. Harvey, Director of the Vaccine Department of the R. A. M. College throughout the war, and they resulted in establishing the points that

a sufficiently large dose of para. "A" and para. "B" vaccine could be added to the customary dose of typhoid vaccine without causing reactions appreciably more severe than those of T. V. by itself, and without interfering with the satisfactory development of typhoid immune substances in the blood of inoculated animals and inoculated men. As regards the development of immune substances against the two paratyphoid organisms, this was also regarded as fairly satisfactory, though here they had no effective standards to work by, while the actual degree of protection against paratyphoid infection had obviously to be left for future decision from statistical evidence.

The actual formula of the mixed vaccine determined upon, and used for the rest of the war, was as follows:

| Bacillus | 1st Dose | 2nd Dose |
|----------------------------|--------------|----------------|
| <i>B. typhosus</i> | 500 Millions | 1,000 Millions |
| <i>B. paratyphosus</i> "A" | 375 Millions | 750 Millions |
| <i>B. paratyphosus</i> "B" | 375 Millions | 750 Millions |

As to the results of mixed vaccine, Leishman concludes that they were clearly successful in securing to the army a considerable measure of protection against paratyphoid infections, in addition to that against typhoid itself, the protection against the former being of a lower grade than that against the latter.

Inoculation with T. V. alone had conferred an appreciable degree of protection against paratyphoid, in addition to the marked immunity it gave against typhoid. The figures, as far as they go, appear to show a more pronounced effect of the vaccine upon the severity of the attack, as judged by the case-mortality, and this appears to strengthen considerably the assumption that the typhoid vaccine had given some immunity against paratyphoid.

The generally mild nature of an attack of enteric fever in an inoculated man is now well recognized, and, particularly in the case of typhoid fever, has greatly added to the difficulties attaching to a diagnosis made solely on the clinical evidence. Although inoculation does not modify a subsequent attack of paratyphoid to

anything like the same extent, yet here, too, there are encountered many cases so mild, or so atypical, that only prolonged and careful laboratory work can establish their true nature. It results from this, that unless all cases of continued fever, of whatever nature, are subjected to an examination as thorough and exhaustive as in the case of a definite "enteric suspect" an unknown number of mild infections with typhoid and paratyphoid fever may escape detection.

In the double infections, the author states that the task of laboratory confirmation, however, remained a very difficult one owing to the fact that, in the case of men who have had "T. A. B." vaccine, the agglutination titers of their serums are often raised not only against the bacillus, which is the cause of their attack, but against the others as well, though usually to a less marked degree. Still, making every allowance for this, cases were not uncommon in which the curves built up from the recorded estimations of the three agglutination indices were very suggestive that more than one of the group had been at work.

It was also found that inoculation appears to have diminished the chances of successful isolation of the bacilli from the blood at the time when this would be of the greatest service from the diagnostic point of view, namely, the early stage of the fever. This influence of inoculation in the inhibition or diminution of the degree of bacteremia was illustrated in a striking manner on several occasions.

In regard to the use of vaccine in the treatment of enteric fever, it was found that the favorable results occasionally obtained were too inconstant and that the method as a whole was too little under control to justify dependence being placed upon it as a routine measure.

Inoculation in Presence of Epidemic. A. Romanes and G. G. Johnstone⁷ report upon the "Value of Extensive Inoculation of a Community During an Epidemic of Typhoid Fever," saying that doubt can no longer exist concerning the incalculable value of anti-typhoid inoculation as a means of preventing typhoid

(7) British Med. Jour., Dec. 18, 1920.

fever in military communities. The published figures of the incidence of typhoid fever in all armies during the late war prove this point conclusively. In this case the inoculation has almost invariably been carried out under favorable circumstances and in the absence of an epidemic prevalence of the disease.

The question arises as to the value of inoculation as a means of protection—first, to the individual, and secondly, to the community as a whole—during an actual epidemic. The opportunities for the study of this subject on a scale large enough to give any reliable results have been few.

The inoculation at Ostend was the first instance of compulsory inoculation applied to a large general community. The object of the authors is to put on record another similar case of compulsory inoculation which occurred in the winter, 1918-19, shortly after the armistice. On the arrival of the British Army of Occupation in Germany, it was found that at Euskirchen, a town of 13,000 inhabitants, there was a considerable outbreak of typhoid fever. In addition to the outbreak at Euskirchen itself, there were two other minor outbreaks in groups of surrounding villages.

It is unnecessary to detail all the inquiries which were made to trace the origin of the epidemic—the water supply, the milk supply, butter, etc. All these points were investigated. The investigations led to no definite conclusion. Most of the cases were probably of contact nature, and the original source of infection was not discovered.

Inoculation of the civil community was performed in each of the three districts where the outbreaks occurred. The vaccine used contained in 1 c. cm.:

| | |
|---------------------------------|----------------|
| <i>B. typhosus</i> | 1,000 millions |
| <i>B. paratyphosus A.</i> | 500 millions |
| <i>B. paratyphosus B.</i> | 500 millions |

The routine method in the British Army was followed of giving two doses at intervals of ten days. It was decided that all persons between the ages of 6 and 45 years

should be inoculated, with the exception of those certified by a doctor to be suffering from an ailment which contraindicated such treatment and of women three months before and two months after childbirth. The doses were graduated according to age—the first dose being as follows:

| | | |
|---|-------|-------|
| For persons between 6 and 10 years.... | 0.125 | c.cm. |
| For persons between 11 and 17 years.... | 0.25 | c.cm. |
| For persons between 18 and 45 years.... | 0.50 | c.cm. |

There were 199 cases of typhoid fever in the three epidemics in the town and villages of a combined population of about 20,000, and of these patients thirty-four died—approximately 17 per cent.

Four of these deaths occurred in people who had been recently inoculated twice. The onset of the disease began within the first twenty-four hours after the second inoculation (two cases), on the eighth day after, and on the nineteenth day after the second dose. Two other deaths occurred in cases after the first inoculation, and in each case the symptoms began within the first twenty-four hours. There were altogether thirty-eight cases of typhoid following inoculation, and among them there were six deaths—that is, mortality, 15.7 per cent. With the exception of these six deaths practically all these cases were of a light nature.

Typhoid Mortality of American Cities. *The Journal of the American Medical Association*⁸ presents its ninth annual report of typhoid in the large cities of the United States in 1920.

Every one of the twelve largest cities in the country (Group I) had a typhoid death rate under 10 in 1920, indicating that the remarkable record of 1919 is being maintained. What is still more noteworthy is that while last year ten of the twelve cities had a rate under five in 1919 but seven of these cities recorded a rate under five. In only two instances is the 1920 typhoid rate higher than that for 1919. The most marked declines are reported in Baltimore, Pittsburg and St. Louis.

(8) March 26, 1921.

**DEATH RATES FROM TYPHOID IN CITIES OF GROUP 1
(MORE THAN 500,000 POPULATION)**

| | Deaths from Typhoid per 100,000 Population | | | | |
|-----------------|--|------|----------------------|----------------------|----------------------|
| | 1920 | 1919 | Average 1916-1920 | Average 1911-1915 | Average 1906-1910 |
| Chicago | 1.1 | 1.2 | 2.4 | 8.2 | 15.8 |
| Boston | 1.5 | 2.2 | 2.5 | 8.0 | 16.0 |
| New York ... | 2.4 | 2.0 | 3.2 | 8.0 | 13.5 |
| Los Angeles .. | 2.6 | 4.7 | 3.6 | 10.7 | 19.0 |
| St. Louis | 2.7 | 5.8 | 6.5 | 12.1 | 14.7 |
| Pittsburgh ... | 2.7 | 6.2 | 7.7 | 15.9 | 65.0 |
| San Francisco.. | 3.1 | 3.3 | 4.6 | 13.6 | 27.3 |
| Cleveland | 3.2 | 2.4 | 4.0 | 10.0 | 15.7 |
| Philadelphia. . | 3.3 | 4.4 | 4.9 | 11.2 | 41.7 |
| Baltimore | 4.7 | 8.9 | 11.8 | 23.7 | 35.1 |
| Detroit | 5.1 | 5.3 | 10.6 | 18.1 | 21.1 |
| Buffalo | 5.1 | 7.0 | 8.1 | 15.4 | 22.8 |

For the first time since these annual summaries were begun, the averages for three full five-year periods are available for comparison. In every city in Group 1, a sweeping reduction in typhoid mortality has occurred. In the first quinquennium (1906-1910) all 12 cities had an average typhoid rate of over 10; in the second, nine or all but three had a rate over 10, but in the third only two of the 12 had an average rate over 10. In 1919 and 1920 not a single city in the group had a rate as high as nine. The saving of life through the general reduction of typhoid mortality can hardly be dwelt on too often. Pittsburg, for example, if the average typhoid rate for 1906-1910 had been maintained in 1920, would have lost last year 382 of its citizens from this disease instead of sixteen.

In going over the reports and discussion of typhoid in various cities, one is impressed with the relative frequency of small outbreaks—sometimes hardly half a dozen cases—attributable to drinking the contaminated water of rivers, small streams or springs in public parks or recreation grounds. Oftentimes the water drunk at a "picnic party" is from a source so obviously and so badly contaminated that only the very young or very ignorant would think of using it. In addition to the precaution of making such sources as difficult of access as possible, it would seem that educational influence

must be largely relied on to prevent this mode of infection.

A comparison of the "Honor Roll" (typhoid death rate from 0.0 to 2.0) for 1920 with that for 1919 shows that the number of cities with the lowest rate has increased from eight to ten. Three cities, Chicago, Scranton, Pa., and Tacoma, Wash., are on the Honor Roll in both years. Cambridge, Mass., has the distinction of making the best record of any American city for the whole fifteen-year period.

Typhoid Outbreak in Salem. The extensive typhoid-fever outbreak at Salem, Ohio, is reported in a special article⁹ and by W. H. Bunn.¹

Beginning about the middle of September and continuing well into October (1920), Salem was in a grip of an epidemic of enteritis which affected at least 65 per cent. of the population. Most of those affected were only temporarily incapacitated by the diarrhea and vomiting, while many suffered only the inconvenience attendant on these symptoms of the ordinary mild attack of enteritis. However, a considerable number had headache, pain in the back, aching muscles and an elevation of temperature ranging from 99° to 101° F. for from twenty-four to forty-eight hours. This group had a convalescent period of from two to three days.

Salem is a manufacturing town of about 10,300 population. For five years prior to 1920 there had been almost no typhoid, with the exception of eight cases in the autumn of 1918, shown to be due to a contaminated milk supply. No case was reported between August, 1919, and August, 1920. A total of 882 cases occurred within a period of three months, beginning on October 2, distributed as shown on the chart (Fig. 24).

The general sanitary conditions of Salem are about what are generally found in towns of this size. The water supply, about 800,000 gallons daily, comes from several groups of deep wells. The water is pumped from the wells and is run by gravity lines to a covered reservoir, from which it is pumped into the city mains. Analyses had been regularly made by the state board of

(9) Jour. Amer. Med. Ass'n., Nov. 27, 1920.

(1) Ibid., April 23, 1921.

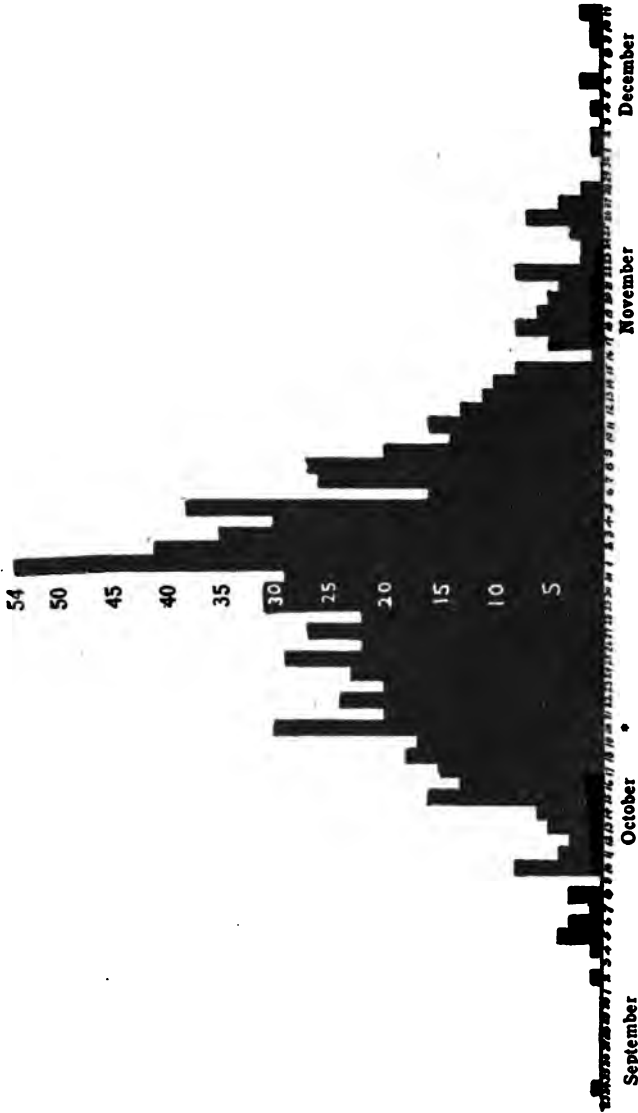


Fig. 24. Incidence of typhoid: Each black block represents a case of typhoid fever charted on the basis of the day the patient went to bed. At the point marked by the asterisk, the water was chlorinated.

health, and the supply has been regarded as excellent from a hygienic standpoint.

The milk supply is distributed through half a dozen dealers, two of whom deliver pasteurized milk—about two-thirds of the total supply. This is a very creditable showing for a city the size of Salem. The city sewage is treated on intermittent sand filters, from which it runs into Beaver Creek, a tributary of the Ohio River. To a certain extent and particularly on the outskirts of the city, privies are in use. There are about 400 of these. Dug wells are present on about 200 premises, but many have not been used for drinking purposes. It is believed that close to 100 per cent. of the population have access to city water at some time during the day.

During the latter part of August and the early part of September of 1920, three cases of typhoid fever are now known to have occurred. Following a rainy period in the latter part of September and particularly during the first part of October, enteritis was prevalent in the town. An emergency chlorinating outfit was installed October 20. Notices advising the boiling of drinking water were also sent out.

The epidemiologic investigation revealed the almost universal incidence of enteritis, which could be accounted for only by a pollution of the public water supply. Samples of water taken from a number of points on the distribution system showed gas within a few hours. Samples of water from the wells which furnish the city's supply showed no contamination. Evidently the pollution was taking place at some point in the collecting or distributing systems. Further investigation of the water supply had also been made by the state department of health, in which it was found that one of the gravity lines connecting one group of wells with the reservoir was polluted. This line was immediately cut off.

The incubation period averaged fourteen days. This conclusion is deducted from the fact that the greatest concentration of typhoid organisms in the water occurred, October 18 and 19, the two days previous to the chlorination of the water. From this time until Novem-

ber 1, the day on which the greatest number of patients took to bed, is just two weeks. Further proof is found in the case of a high school football player mentioned, who took to bed just fourteen days after definite exposure.

Bunn says that the most important fact which we gather from this epidemic is that connected with the effectiveness of anti-typhoid inoculation. On the age incidence chart kept by the state epidemiologist, a discrepancy was found on the male side between the ages of 20 and 30. In seeking an explanation for this, statistics on the number of ex-service men in the town were collected. It was found that among the 210 ex-service men there were only three cases, or an incidence of 1 in 70; while among the entire female population between the ages of 20 and 30 the incidence was eight. Records as to the time since vaccination, collected by the American Legion at the request of Mr. R. A. Tarbett of the United States Public Health Service, show that all the ex-service men had been vaccinated for more than two years, and some of them as long as three years. This is definite proof that an individual enjoys a considerable degree of immunity for at least two years after inoculation.

The lessons for other communities to be learned from this epidemic are not new, but they are frequently forgotten. The most important is the necessity for constant supervision of every water supply, however pure its origin.

Blood Cultures in Typhoid. In Richmond, Virginia, the health department laboratories now make several hundred blood cultures for typhoid bacilli yearly, according to A. H. Straus.² The blood cultures are made in the main by practicing physicians who make use of material furnished by the department.

The outfit consists of two bottles of media, one of peptone bile (plain ox bile to which 1 per cent. peptone has been added) and one of beef infusion bouillon to ~~1~~ 1 per cent. sodium citrate and .009 per cent. salt added.

Straus sums up his conclusions as follows:

First, the dried drop Widal test should be discontinued because it is unreliable and more misleading than helpful.

Second, the blood culture is a valuable test not only for ideal conditions in a hospital, but also for routine work by practicing physicians in the cities and possibly in the rural districts as well.

Third, the macroscopic Widal test is simple, practical and reliable. Fourth, stool examinations should be available when needed.

MALARIA

Science and Practice in Fight Against Malaria. B. Gosio,³ director of the Laboratory of Micrography and Bacteriology of the Department of Public Health, Rome, in reviewing the fight against malaria states that in Italy during the period from 1887 to 1902, immediately preceding the enforcement of the antimalarial laws, the records show an annual average of 15,000 deaths, while during the three years 1903 to 1905, which saw the beginning of this enforcement, the average fell to 8,000, and then to 3,700 from 1906 to 1912, to 2,664 in 1913 and again to 2,045 in 1914.

The points which he emphasizes in antimalarial work are the treatment of the cases and adequate organizations to carry on the prophylaxis work in all communities where the disease is prevalent.

He states that to delay the death of a malarial patient, without curing him, is to add to the number of carriers and to enlarge, for the healthy, the dangerous area.

Malaria Awakening in the South. Referring to the enormous agricultural and business growth that it taking place in the South at the present time, L. D. Fricks⁴ states that this can be permanently checked by only one thing—malaria.

He believes that the opinion of H. R. Carter, that actual malaria-control demonstrations and the education of the children in the public schools are the only educa-

(3) New Orleans Med. and Surg. Jour., November, 1920.

(4) Jour. Amer. Med. Ass'n., Sept. 25, 1920.

tional measures now being employed which are of general practical value in impressing on the individual or community the importance of malaria control as a health measure, is probably correct.

He believes also that the health officers of the Southern states should undertake to secure such legislation as may be necessary to prevent the increase of malaria, resulting from agricultural and industrial development—"man-made malaria," as Dr. Carter calls it—particularly in relation to (1) drainage projects, (2) highways construction, (3) new construction of railroads, and (4) impounded waters. The state health officer should be given proper legal authority to advise in the planning of these new projects so far as they may affect malaria prevalence.

Coöperative Antimalaria Campaigns. J. A. LePrince⁵ states that the success of the experimental demonstration campaigns carried on in Arkansas for several years have shown the wisdom and advisability of extending such operations to other states where elimination of malaria is of the utmost importance to the proper normal development of the state and the welfare of its citizens.

With this in view, a coöperative agreement for undertaking malaria-control campaigns was made by the state health departments of ten states, the International Health Board and the United States Public Health Service.

The state health officers of Alabama, Arkansas, Georgia, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, Texas and Virginia wisely undertook malaria-control work under this coöperative plan.

Several facts of importance have been brought out. The most important is the necessity of sufficient proper publicity to create a demand on the part of citizens, influential organizations and associations of interests, so that specific state appropriations for malaria control may be made available. Other points of importance are:

That drainage operations be so planned as to be practically concluded before the mosquito season opens.

A definite plan should be made by each state health department to take a malaria census the year before

(5) Southern Med. Jour., April, 1921.

control measures are instituted and again directly after the close of the season's operations.

In towns where antimalaria work is undertaken the public quickly gets the impression that the scope of the work will be such as almost to eliminate the mosquito pest of previous years, and many persons condemn the work when such results are not achieved. It appears essential to advise the public properly when the work is first started that it will cost the community much more to get a practical freedom of mosquitoes than to eliminate *Anopheles* only, due to the additional cost of inspecting back yards, etc.

Malaria in Texas. H. J. Ehlers⁶ states that in the period from 1910 to 1919 there were 3,509 deaths, or an average of 350.9 deaths *per annum*. The 3,509 deaths for the ten years amount to a loss of 10,527,000 (3,509x3,000) work days. This represents a financial loss of \$21,054,000, estimating the cost of labor at \$2 a day.

He describes the work of the Antimalaria Demonstration Unit which is along well-established lines.

The *per capita* cost in the twelve towns amounted to 70.7 cents for the year 1920.

The malaria reduction based upon the number of physicians' calls ran 31, 55, 65 and 66 per cent. in the four towns respectively.

Destruction of *Anopheles* in Dwellings. D. L. Van Dine⁷ reports his results of *Anopheles quadrimaculatus* collections from inside screened dwellings over a period of several years at Mound, La., located in the delta region of the lower Mississippi Valley and under prevalent malaria conditions.

The conclusion is that under the conditions of this region screening does not give complete protection from *Anopheles* and that those which gain entrance to the dwellings should be regularly destroyed by the simple method suggested by the Panama experience, supplemented by the use of pyrethrum powder. A further conclusion is that *Anopheles quadrimaculatus*, at least, deprived of a blood meal at nightfall or later, will bite

(6) Med. Insurance and Health Conservation, February, 1921.

(7) Southern Med. Jour., April, 1921.

any time of the day or night when temperature conditions are suitable and the opportunity offers.

Slides for Malaria. J. S. K. Boyd⁸ gives the following method of examining blood for malaria. A large drop of blood is received on a clean slide and spread over an area one-half inch square. This is dried with moderate heat and then covered with this solution :

| | |
|--------------------------|----|
| Formalin | 20 |
| Glacial acetic acid..... | 2 |
| Distilled water | 78 |

Leave this on for 10 minutes, wash with tap water and stain with borax methylene blue or Loeffler's methylene blue for 2 minutes. Wash in tap water. Do not blot. Dry with heat. The background is stained greenish, the leukocytes and parasites blue.

YELLOW FEVER

Distribution and Control of Yellow Fever in 1920. W. C. Gorgas, H. R. Carter and T. C. Lyster,⁹ of the Yellow Fever Commission of the International Health Board, Rockefeller Foundation, present maps showing the location of endemic and epidemic areas of yellow-fever infected areas in November, 1920, and in previous periods. The maps for the eighteenth and nineteenth centuries, 1899-1900, 1905-1906, and November, 1920, are herewith reproduced, and together with the legends are self-explanatory (Figs. 25, 26, 27 and 28).

The authors state that Bolivia is the only country in the Western hemisphere, so far as is known, that has not been visited at least once by yellow fever, and some countries have been visited many times. The reason that Bolivia has escaped is due to its having no coast line or low altitudes; hence, no stegomyia.

The principal preventive measures in the fight against yellow fever are enumerated, as follows:

- (a) *Prevention of Introduction:* (1) quarantine; (2) immunity by lowering stegomyia index.

(8) Jour. Royal Army Corps, October, 1920.

(9) Southern Med. Jour., December, 1920.

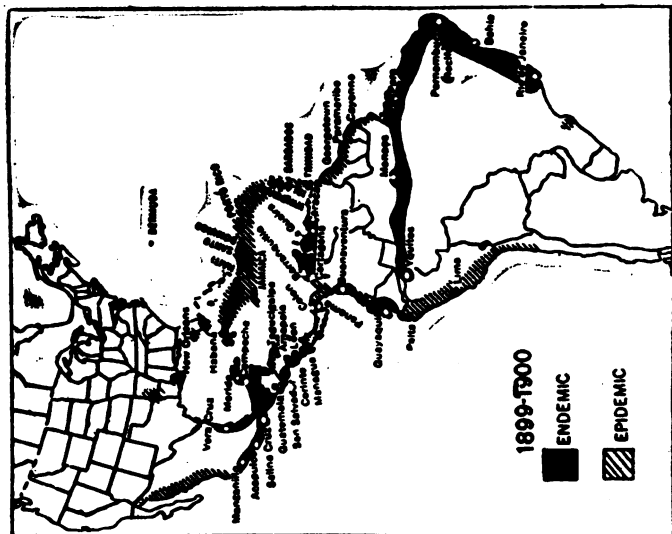


Fig. 26. In 1899 and 1900, due largely to the change from sail to steam, the areas had contracted, especially at the upper and lower limits, leaving the central areas much as of old.

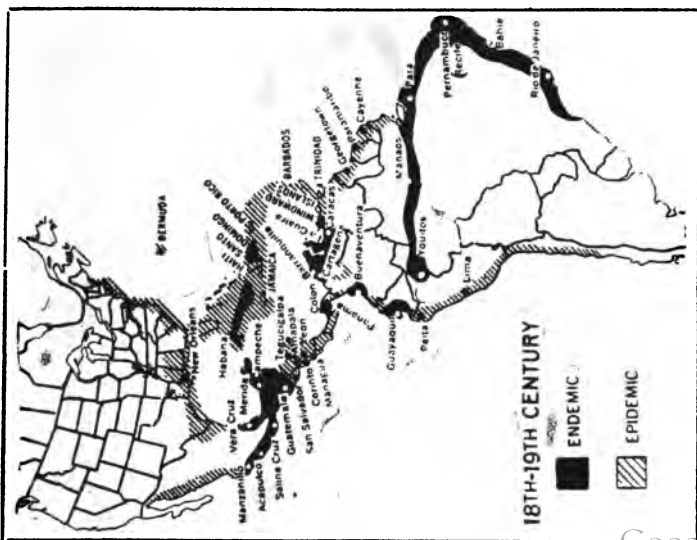


Fig. 25. During the nineteenth century epidemics occurred as far south as Buenos Aires and as far north as Montreal.

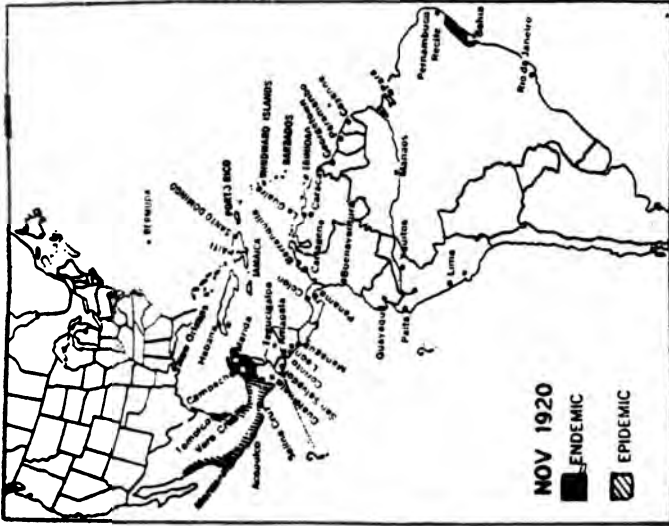


Fig. 28. Nov. 1, 1920.—Since this article was written, in June, 1920, the epidemic area of Central America has widened to include Guatemala and Nicaragua and again has contracted to a small area in Salvador which is approaching elimination. The epidemic area in Peru also has about reached the point of elimination. The epidemic area of Mexico has widened to include its total coast line and southern border.

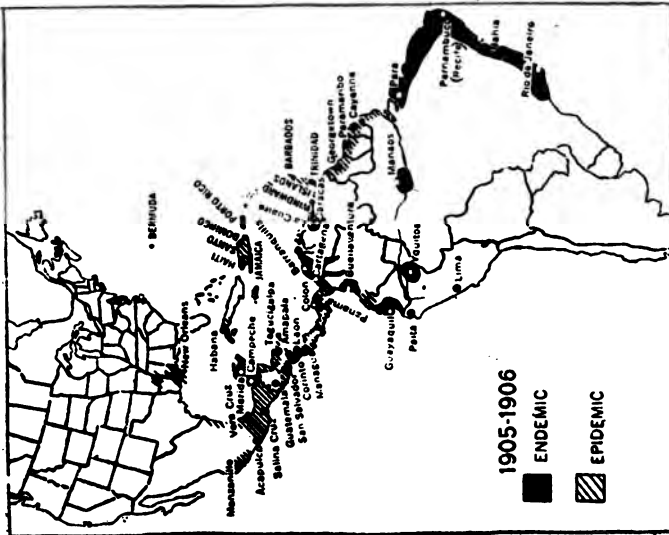


Fig. 27. In 1905 and 1906, knowing then the role played by the stegomyia in the distribution of yellow fever, the endemic center of Havana had been freed, resulting in the epidemic areas in Chile, Peru, the United States (Louisiana excepted), and most of the West Indies, either freeing themselves through natural causes or by the use of sanitary measures.

(b) *Elimination*: When, however, yellow fever has gained admission to a country, the methods of elimination will depend upon the efficiency of its sanitary organization.

1. *Fumigation*: The first choice has usually fallen upon fumigation, the most unsatisfactory of all.

2. *Isolation*: The early isolation of yellow fever patients has always been and still is most desirable, but it is most difficult to accomplish.

3. *Vaccines and Serums*: The brilliant work of Noguchi in discovering the organism causing yellow fever (*Leptospira icteroides*) already is having some effect on the control of the disease.

4. *Anti-stegomyia Measures*:

Prophylactic Inoculation. H. Noguchi and W. Pajera¹ state that sufficient grounds for the possibility of establishing a prophylactic vaccination against yellow fever are furnished by the facts that (1) a person acquires a state of complete immunity enduring for a period of years after recovery from an attack of yellow fever; and (2) the serum of such a person, and also of guinea-pigs once inoculated with the blood of yellow fever patients, contains varying amounts of anti-bodies against *Leptospira icteroides*. That such vaccination is a distinct possibility is shown by their experiments.

From the results of vaccination in guinea-pigs, it may be concluded that when sufficient quantities of the killed culture are given, these animals are usually rendered resistant to a subsequent infection with *Leptospira*. The degree of protection, however, is not strictly proportional to the amount of the vaccine inoculated.

As regards the vaccination of human beings, thus far the results are distinctly encouraging; but the authors realize that many more observations will be needed before a final decision of its value can be arrived at.

HOO KWORM

Hookworm in Mines. An interesting observation is that of R. W. Nauss² that hookworms are not found in

(1) Jour. Amer. Med. Ass'n., Jan. 8, 1921.
(2) Amer. Jour. Pub. Health, May, 1921.

certain gold and copper mines. Analysis shows this freedom from infestation is due to the presence of from 1 to 2 per cent. chlorides as chloride in the soil.

Boycott and Haldane report the same condition due to the same cause in under-the-sea Cornish mines, and Manouorix and Calmette in certain French mines.

The hookworm larvae just as they emerge from the egg are delicate and easily killed. At other stages they are not.

Salting the floor of mines as a preventive measure is not practicable except under occasional conditions. Nauss found that ankylostoma infection of miners in certain mines in California was due to infection of the soil of the mine floor.

Endemicity of hookworm infection of a mine was greatly influenced by temperature, humidity and mine drainage. The use of mine water catchment devices and storage tank reservoirs to receive evacuations of men under ground may be responsible for a low incidence of infestation. Where men defecate along streams in the floors of mines the larvae are rapidly spread along the course of the stream.

[The observation by Nauss confirmed by the British and French observers suggest the possibility of the use of salt or hypochlorite in domestic privies to control hookworm infection.—ED.]

VENEREAL DISEASES

Programs for Venereal Disease Control. The huge, country-wide experiment that has been carried on for the last two or three years has resulted in fixing certain definite lines of activity as fundamental to any complete program of venereal disease control.

According to Millard Knowlton,³ Regional Consultant, United States Public Health Service, such a program should include the following activities:

1. Treatment of existing cases to render them non-infectious.

2. Administrative measures of control by the health officer.

(3) Nation's Health, June, 1921.

3. The repression of prostitution for the purpose of cutting off the supply of infection.

4. Educational measures directed toward giving higher standards of sex conduct and disseminating information concerning the ravages and prevention of venereal disease.

Is Progress Being Made in Venereal Disease Control? C. C. Pierce,⁴ speaking particularly of conditions in Illinois, points out that whereas two years ago treatment for syphilis was beyond the means of the average man, today there exists a network of 500 odd clinics stretching from coast to coast where free examinations are carried out and where free treatment for gonorrhoea and for syphilis is given. There are also twenty-six clinics in Illinois where free treatment for venereal diseases is obtainable. Seventeen of these twenty-six clinics, however, are located in Chicago.

In most communities there are sufficient laws to curb open prostitution and the great need in Illinois as elsewhere is for more efficient law enforcement. Let the physicians be among those who demand that such laws be not a dead letter.

Lessons Taught by Venereal Disease Control Measures. From a study of the work during the past two years, C. C. Pierce and H. F. White⁵ conclude:

1. It is absolutely essential that a three-phase program be carried on for the successful control of venereal diseases. The three phases of the work are medical, legal and educational.

2. More attention must be paid to preventing infection.

3. There must be devised and inaugurated a comprehensive, constructive, practical plan for sex education so that the method can be applied in schools, beginning in the early grades and continuing through high school and college.

Recent European Venereal Disease Measures. The Norwegian law, which came into force Jan. 1, 1919, embodies far-reaching provisions limiting the spread of venereal diseases.

The marriage of persons suffering from syphilis in the

(4) Ill. Med. Jour., June, 1921.

(5) Jour. Amer. Med. Ass'n., Oct. 23, 1920.

infectious stage is prohibited. In connection with the publication of the banns, each of the prospective parties to the marriage contract must give a written declaration to the effect that syphilis is not present in an infectious stage, and whether or not any other venereal diseases still in an infectious stage or epilepsy or leprosy exists.

When either of the prospective parties to marriage suffers from venereal disease, epilepsy, or leprosy, the authorities celebrating the marriage must be assured that both parties have received instruction from a physician as to the dangers entailed. In this connection a medical certificate is required. The law also refuses to recognize the privilege of professional secrecy in these matters; medical evidence may be called in litigation involving marriage, and a physician who knows that a person contemplating marriage suffers from any of the above diseases is bound to communicate his knowledge to the authorities concerned.

Some of the difficulties encountered in Liverpool are commented on by the *Medical Officer*.⁶

Facilities for accurate diagnosis by general practitioners and free treatment of those affected are the basis of the scheme of prevention. The cost has been heavy, but apparently the full value of the expenditure involved has not been obtained, because of the very unsatisfactory circumstance that no less than 60 per cent. of the patients discontinue treatment before they are free from infection. The same story is related in many other districts.

Compulsory detention has been suggested for this condition, but the *Medical Officer* is of the opinion that the time has not yet arrived for this measure and believes its application now would defeat the object in view, for it would act as a deterrent in seeking advice and treatment in the first instance.

The possibility of suppressing syphilis is considered by Jules Goldschmidt⁷ of Paris. He is of the opinion that with the strenuous coöperation of all civilized nations and with untiring persistence it seems possible at present not so much to eradicate the evil completely, but

(6) Aug. 20, 1921.

(7) Med. Rev. Reviews, March, 1921.

to keep it under strict control. Thus controlled, medical science may some day be able to eradicate it completely.

Legislative Control and Antenatal Syphilis Rate. The incidence of antenatal syphilis is made the basis for judging the effect of legislative control in Australia by J. H. L. Cumpston.⁸

It might be thought that if the venereal disease control legislation were producing the result expected of it, the deaths due to congenital malformations and congenital debility would show a definite reduction in proportion to the births; as it is reasonable to assume for the present purpose that congenital syphilis plays a considerable part in the mortality of the first three months of infant life.

The table presented shows the mortality figures for each of these causes of death and for the sum of the two for a period of ten years, during which the statutes have been in operation in various states for varying periods. The table deals with the mortality in the first three months.

It is obvious from a scrutiny of the figures that no state, whether with or without legislation, shows any improvement throughout the period, either in the one-month or the three-months' period. The relationship of this fact to the administrative campaign against venereal diseases is capable of discussion from alternative aspects. Either the mortality at the ages under discussion is not the result of venereal infections or the measures now in operation against venereal diseases are not materially or favorably affecting mortality from congenital venereal infections.

The fact that 9.75 per cent. of all women attending the maternity department of the Women's Hospital in Melbourne showed a strongly positive Wassermann reaction is, at least, presumptive evidence of extensive congenital infection and, when the examination of neonatal infants shows an almost equal percentage of reactions, it establishes the "persistence of syphilis in the offspring of syphilitic mothers" and appears to dispose effectively of the suggestion that venereal infections play no part in the mortality at the ages under discussion.

(8) *Med. Jour. Australia*, Aug. 20, 1921.

The remaining alternative is of supreme interest to the hygienist who desires success in the attempt to control venereal diseases. If, as appears to be the case, the present measures are not favorably affecting antenatal venereal infections, what is the reason? It would be

COMMONWEALTH OF AUSTRALIA

Total Deaths Under Three Months per 1,000 Births in the Year

| Year | | New South Wales | Victoria | Queensland | South Australia | West Australia | Tasmania |
|------|--------------------------|-----------------|----------|------------|-----------------|----------------|----------|
| 1910 | Malformations..... | 2.21 | 2.54 | 2.60 | 3.28 | 2.77 | 2.69 |
| | Congenital Debility..... | 21.37 | 22.30 | 18.00 | 19.45 | 20.70 | 29.54 |
| | Total..... | 23.5 | 24.8 | 20.6 | 21.6 | 23.4 | 32.1 |
| 1911 | Malformations..... | 2.50 | 2.10 | 2.94 | 3.07 | 1.48 | 2.21 |
| | Congenital Debility..... | 20.99 | 20.19 | 17.19 | 17.18 | 23.00 | 20.42 |
| | Total..... | 22.4 | 22.2 | 20.0 | 20.1 | 23.4 | 22.6 |
| 1912 | Malformations..... | 2.12 | 2.96 | 2.99 | 2.73 | 2.76 | 0.85 |
| | Congenital Debility..... | 21.19 | 21.12 | 18.25 | 21.19 | 22.79 | 25.67 |
| | Total..... | 23.2 | 24.0 | 21.1 | 23.8 | 25.4 | 26.4 |
| 1913 | Malformations..... | 2.13 | 3.003 | 3.45 | 2.46 | 3.04 | 4.42 |
| | Congenital Debility..... | 22.86 | 21.96 | 18.40 | 20.43 | 19.74 | 23.62 |
| | Total..... | 24.9 | 24.9 | 21.8 | 22.8 | 22.7 | 28.0 |
| 1914 | Malformations..... | 2.46 | 3.40 | 2.82 | 3.56 | 3.69 | 1.50 |
| | Congenital Debility..... | 22.91 | 22.56 | 18.46 | 22.01 | 20.1 | 23.1 |
| | Total..... | 25.3 | 25.9 | 21.2 | 25.5 | 23.7 | 24.6 |
| 1915 | Malformations..... | 3.21 | 3.14 | 2.98 | 3.05 | 2.66 | 1.71 |
| | Congenital Debility..... | 23.41 | 25.25 | 19.69 | 22.46 | 19.96 | 28.33 |
| | Total..... | 26.6 | 28.3 | 22.5 | 25.4 | (c)22.5 | 30.0 |
| 1916 | Malformations..... | 3.03 | 3.5 | 3.65 | 3.37 | 3.58 | 2.66 |
| | Congenital Debility..... | 23.08 | 22.81 | 19.88 | 21.00 | 19.39 | 24.64 |
| | Total..... | 26.0 | 26.3 | 23.4 | 24.3 | 22.8 | 27.2 |
| 1917 | Malformations..... | 2.67 | 3.09 | 2.63 | 4.15 | 3.17 | 3.35 |
| | Congenital Debility..... | 21.27 | (a)20.31 | 19.15 | 19.51 | 18.78 | (d)17.11 |
| | Total..... | 23.9 | 23.3 | (b)21.7 | 23.6 | 21.8 | 20.4 |
| 1918 | Malformations..... | 2.86 | 3.45 | 3.74 | 3.17 | 3.52 | 1.89 |
| | Congenital Debility..... | 22.86 | 23.20 | 16.99 | 20.96 | 20.55 | 24.05 |
| | Total..... | 25.6 | 26.6 | 20.6 | 24.0 | 24.0 | 25.8 |
| 1919 | Malformations..... | 2.43 | 3.54 | 2.9 | 3.2 | 4.02 | 1.6 |
| | Congenital Debility..... | 26.8 | 26.8 | 20.3 | 24.0 | 20.02 | 27.6 |
| | Total..... | 29.2 | 30.3 | 23.1 | 27.2 | 24.0 | 29.2 |

Dates on which Venereal Disease Acts became effective: (a) May, 1917; (b) October, 1917; (c) December, 1915; (d) September, 1917.

thought at first sight that the treatment of persons in Western Australia and in Victoria on the scale represented by a notification rate of 113 per 100,000 in the case of syphilis, and of 350 per 100,000 in the case of gonorrhoea, would have had some effect in reducing antenatal infections.

When further it is considered that of the total of notifications approximately 16 per cent. are of married persons, the conclusion can not be avoided that while the present measures are very successful in certain directions, they are not sufficient to prevent the wastage of infant life from venereal infections.

The following additional measures are recommended to supplement the present system of legislative control:

1. Routine examination of the wife (or husband) and the children of the syphilitic.

2. Routine examination of every pregnant woman (which involves compulsory notification of pregnancy) and a proper organization to insure antenatal examination.

3. The provision of facilities at strategic points for effective prophylaxis for immediate application after exposure to infection.

Congenital Syphilis. Congenital syphilis can be cured, but doing so is difficult according to S. Hata.⁹ A far better plan is to treat the syphilitic pregnant woman. When this is properly done the child is born alive and free from syphilitic infection. Hata would like to see every married woman given a Wassermann test and thinks the success of laws compelling the use of silver solution in the eyes of all babies proves that such a proposal might succeed. However, it would be easier to persuade pregnant women to have Wassermanns made and to get those showing positive to take appropriate treatment.

In a large group of married women showing positive Wassermanns he found that 40 per cent. had not been impregnated, 60 per cent. had been. Of the impregnations, 28 per cent. had resulted in abortions, 42 per cent. had resulted in children who had died within two years

(9) Inter. Jour. Pub. Health, July-August, 1921.

(58 per cent, of living births), and 30 per cent. in children living more than two years (42 per cent. of living births). Statistics show, he says, that not over one-third of the children born to mothers presenting positive Wassermanns and surviving birth more than two years live "a natural course of healthy life." Some become blind from parenchymatous keratitis, others deaf from otitis, others have juvenile tabes, epilepsy, imbecility.

By early treatment of congenital syphilis a negative Wassermann has been obtained. By late treatment this is never possible. In a study of the Wassermann test in women the following results were obtained:

In Group 1, composed of married women who do not admit syphilis in husbands, 21 per cent. gave positive Wassermanns.

In Group 2, married women unaware of being syphilitics but admitting that their husbands were, 52 per cent.

In Group 3, married women aware that both they and their husbands had had syphilis, 27 per cent.

In Group 4, unmarried women unaware of having syphilis, 50 per cent.

In Group 5, unmarried women aware of having syphilis, 50 per cent.

He concludes that strenuous effort should be made to make Wassermann tests on pregnant women. Those giving positive Wassermanns should be given anti-syphilitic treatment without delay. The new-born babe should be examined by the Wassermann test; if this is positive, treatment should be begun at once. If either husband or wife should have syphilis the blood of the other should be examined.

Increase of Venereal Diseases in the American Army after Armistice. The increase of venereal diseases in the army after the armistice is the subject of a paper by T. W. Satterthwaite.¹ He quotes Dr. J. E. Moore, consulting urologist in Paris, as stating that at one time the incidence of infection in the American Expeditionary forces from some kind of venereal disease was about 330 in a thousand, *i. e.*, about one in three. Also, that in August and September, 1917, the incidence among 5,000 British troops in Paris was 200 in a thousand. The ratio

(1) New York Med. Jour., Oct. 30, 1920. Digitized by Google

alluded to above by Moore was said to be four times greater than elsewhere among our men in zones occupied by them, the inference being that special efforts were capable of reducing the disease, if proper measures were adopted.

Ettie A. Rout² reports that Captain Walker said he had not found one case of venereal disease contracted in a licensed house in the city of Paris, and she could only suppose that the people who were responsible for putting the licensed houses in Paris out of bounds knew nothing at all about the real facts of the case. In the licensed houses of the city of Paris during the year 1917, only five cases of venereal disease were contracted, and in 1918, up to April 20 (the day she was speaking), there had not been one case of venereal disease contracted in a licensed house in the city of Paris. (Of course, the Paris houses were well conducted and medically supervised.)

Out of 200 women arrested on the streets of Paris during the month of April, 1918, over 25 per cent. were found to be infected with venereal disease. But this was much better than in 1917. In the months of November and December, 1917, the French authorities had a round-up on one boulevard of seventy-one women, of whom fifty-five were infected. A few days later about 100 women were arrested, and 91 per cent. were found to be infected with venereal disease.

Nevertheless, the Americans put the Paris licensed houses out of bounds to their soldiers, and the men consorted with the much more dangerous women of the streets. The British order in this respect was never enforced.

INDUSTRIAL HYGIENE

Rise, Progress and Opportunities. Sir Thomas Oliver,³ in an address before the eighty-ninth annual meeting of the British Medical Association, gave a comprehensive survey of the advancements of industrial hygiene and outlined the problems of the future. He pointed out

(2) New York Med. Jour., Jan. 8, 1921.

(3) Brit. Med. Jour., July 23, 1921.

that it is just over a century ago since the British Parliament turned its attention to the fate of children employed in the mines and factories of that country, and little more than half a century ago since diseases due to occupation received similar recognition.

While the introduction of machinery made labor in the factories in one sense less irksome, it led to the employment of women and children, many of whom, owing to the long hours and low wages, rapidly broke down in health, with no financial assistance from the State or from the industry to fall back upon, so that to ill health were added the distressing circumstances of poverty and starvation with only the workhouse to look forward to.

Industrial hygiene may be said to have merged out of, or to have been a continuation of, parliamentary interference with the claims of employers to utilize labor almost to its breaking point. Society, in the past, kept itself too far aloof from knowledge of the conditions under which certain trades were carried on, and even the workers themselves were not always aware of the dangers to which their employment exposed them.

He reviews the progress made in the prevention of lead, phosphorus and carbon monoxide poisoning and the effect of industrial hygiene on the health of miners.

Lead poisoning cases in Great Britain in the pottery industry in 1900 numbered 200, as compared with eleven in 1918; in the paint and color works industry the numbers being fifty-six in 1900, as compared with three in 1918.

The figures for lead poisoning cases in 1919 are slightly higher. This, he attributes, to the reduced vitality of workers recently returned from the war.

As to phosphorus poisoning he points out that beyond an occasional dermatitis arising in workers as a result of contact with the sesquisulphide of phosphorus, the whole industry has become transformed from a dangerous to a harmless trade.

The fatal accidents in coal mines have been reduced two-thirds since 1851. The number of miners killed in 1851 being 4.35 per 1,000 as compared with 1.37 per 1,000 in 1912.

Recently much progress has been made in the study

and prevention of fatigue. The important findings which Oliver considers are the following:

It is now generally admitted that fatigue is the result of the action upon the tissues of such poisonous substances as carbon monoxide and lactic acid formed by the chemical dissolution of the glycogen of over-worked muscles. These bodies act not only upon the muscular tissue itself and the nerve endings in the muscles, but since they find their way into the blood-stream they poison the higher nerve centers in the brain, thus converting fatigue, the outcome primarily of localized changes in the neuromuscular apparatus, into a general state of the organism, and of these two forms of fatigue, central and local, the central or general fatigue is the more important.

It is known that the transferece of blood from a fatigued to a healthy animal produces symptoms of fatigue in the receiving animal. Following up this fact, Burkard has demonstrated the presence of a leukocytosis in the blood after exhausting work—a form of leukocytosis which Grawitz named myogenous.

Oliver believes that there is a psychology of industry just as there is a physiology. Psychology is no longer simply "the science of mind or soul," but "the science of the facts of human nature and behavior," and there is no department of human activity which offers greater scope for its study and application than industry.

He urges that the subject of industrial hygiene be given proper attention in the medical colleges, believing that in the ever-enlarging sphere of industrial enterprise, to which the various sciences are contributing, and the needs of the world are calling for, lies the opportunity of industrial hygiene.

Importance of Industrial Medicine. E. L. Collis⁴ says that the benefit to the community is closely interlocked with the benefit to industry, since the community is composed of constituent groups, among which the industrial group (using the word industrial in its widest sense) forms the greatest part.

He points out that in Great Britain the army recruiting examinations disclosed that only 36 per cent. of the

(4) *Lancet*, Sept. 3, 1921.

male adults of age to bear arms were classed as Grade I; but the numbers attaining this standard were found to vary widely according to occupation; the miner and the agriculturist provided a far higher proportion than other groups of industrial workers. He calls attention to the comparative mortality figure of agricultural laborers, which is 470, as compared with printers, 773; tailors, 799; cotton operatives, 811; shoemakers, 820; iron and steel manufacturers, 837; Lancashire coal miners, 941; edged toolmakers, 1,010; costermongers, 1,507; and for general laborers, 2,301.

There is, then, a wide field of work before industrial medicine to establish the why and wherefore of these differences. There is an inclination to associate the subject of industrial medicine only with occupational diseases. The scope of the work has enlarged much beyond the boundaries of occupational disease. Today industrial medicine is recognized to be directly aimed at preventing disease and maintaining health. In industry more easily than elsewhere in the community can the balance be cast between the debit sickness and inefficiency and the credit of health and productivity.

The proposition is put forward that industrial medicine properly applied can effect a saving each year on labor turnover of from 60 to 70 millions, on lost time of from 50 to 60 millions, and through industrial convalescence of many millions more. Put the total at 104,000,000 pounds on a conservative estimate. There are today over 40,000 doctors in the kingdom; the cost, if industry employed half the profession and gave each doctor 2,000 pounds a year for whole-time work, would amount to 40,000,000 pounds a year, leaving a handsome balance of 100,000,000 pounds a year. Such wholesale engagement of the profession is not proposed, and indeed is not needed. The figures are only instanced to demonstrate that industry by developing industrial medicine has the promise of great profit while it fulfills a great social service.

Collis says that today our profession stands too much aloof from such thoughts, and does not do enough to impress upon industry that there is a science of medical sociology, the principles of which, if applied to labor

unrest, would give results more certain, more sure, and more enduring than all the remedies evolved from the inner consciousness of political economists.

Industrial Epidemiology. Industrial epidemiology is defined by W. A. Sawyer⁵ as that phase of medicine which seeks to improve the health of individual workers and prevent the transmission of disease to their fellows. In other words, it deals with the protection of industries against the commonly known communicable diseases.

The measures employed and recommended by the author are vaccination against smallpox of all new employes, and vaccination against typhoid, and the usual preventive measures against diphtheria and tuberculosis.

For the prevention of colds and other respiratory infections, the plan suggested is to send home employes who appear ill or have a temperature of 100° F. or over, and who are sneezing and coughing, or have a profuse discharge from the nose.

Also, employes should be made to feel that both syphilis and gonorrhea will be dealt with like other diseases, and in communities where a venereal disease clinic does not exist, arrangements should be made to treat all such cases properly. Employes should not be discharged or laid off as a penalty when it is discovered they have such diseases. They should know that they can be taken care of in a proper way by a reliable physician, and that their job is secure. If this attitude is not taken they will not come for aid, but will continue at work, perhaps only partially treated and without knowing the proper precautions to take for the protection of others.

Industrial Hygiene and Home Environment. Robert Olesen⁶ is of the opinion that definite though elastic medical and nursing service which extends beyond the factory and office walls is another urgent need in the prevention of industrial tuberculosis as well as other occupational diseases. The barrier which has been erected between the work place and the home must be removed before health hazards can be eliminated in their entirety.

(5) Jour. Amer. Med. Ass'n., Oct. 10, 1920.

(6) Wis. Med. Jour., August, 1921.

Industrial Clinics in General Hospitals. According to Harry Linenthal⁷ the industrial clinic is one of the most important and effective single factors in industrial hygiene. There are several types of such clinics. Some clinics are operated in large manufacturing establishments to render aid to the employes of the particular establishments. Others are conducted outside the manufacturing establishments either by the manufacturer, or on a coöperative basis by employers and employes, or by municipalities, where all workers may apply for medical treatment irrespective of whether the state of ill health from which they are suffering is the result of their work or any other cause. Still another type of industrial clinic is that connected with a general hospital.

The author believes that there is a distinct field for the industrial clinic in connection with a general hospital for the reason that cases of industrial disease present many problems which do not arise in the treatment of the ordinary patient.

Also, there is no agency at present in the community that is so capable as such an industrial clinic, with the aid of the other special clinics in the hospital enabling group diagnosis, of handling the problems that arise in connection with those crippled or made ill by industry. No agency is so well-equipped and able to correlate occupations with the physical condition of the worker and thus serve as a reliable and accurate source of vocational guidance to those incapacitated by industry.

Re-establishment Clinics. J. M. Taylor⁸ says that the enterprise of restoring health by no means ends with the repair of an obvious or urgent ailment. Ill health almost never is a single maladjustment of function, even in the most acute conditions.

The enterprise of readjusting structures and functions, of re-establishing disordered reflexes through influencing the sympathetic as well as the spinal reflexes, is coming to be a large and increasingly significant domain of human betterment. Along with the physical are the mental re-adjustments, needed less or more in every protracted or chronic condition, and in most acute states,

(7) Jour. Amer. Med. Ass'n., March 12, 1921.

(8) New York Med. Jour., July 20, 1921.

especially in those hypersensitive, apprehensive, or bewildered.

Hence in his judgment there should be a special clinic or clearing house to investigate the status of the case in its entirety, while undergoing treatment in any one department.

Routine Physical Examinations. C. K. Ervin⁹ gives his experience and method of physical examinations of workers. He says if physical examinations are conducted with the needs of the employe ever in mind, there can be no objection to them on the part of the men. The greatest cause for complaint in the past has been because of the great number of rejections, which have been as high as 10 and 15 per cent. in some cases. The objection is obviated when provisions are made for placing the handicapped, and the causes for rejection are limited to men whom it would be dangerous to employ, either on account of a danger to themselves, to others, or to property.

The author holds that anything but a complete and careful physical examination is a useless waste of time and energy. This idea should be thoroughly sold to the management.

Few examiners realize that the reaction of the patient to the examination and the type of answers that he gives, is perhaps the most valuable index that the employer can possibly get as to the desirability of the applicant for the job. The physician should so train himself that the employe's reaction to a good physical examination will largely take the place of specific mental tests, which are, in the main, impracticable as applied to industrial workers at large.

Health of Workers in Iron and Steel Industry. An interesting report has been issued by the Industrial Fatigue Research Board of Great Britain, relating to the iron and steel industry. From an abstract of the report in *The Lancet*,¹ the following facts are noted:

The investigation made by Vernon for the Commission disclosed that the steel melters and pitmen lost 23 per cent. more time than the average, the puddlers 20 per

(9) *Nation's Health*, August, 1921.

(1) *Jan. 22, 1921.*

cent. more, the tinplate men 12 per cent. more. Almost all of these men frequently work at high temperatures.

Steel workers showed 102 per cent. greater mortality from respiratory diseases, but 48 per cent. smaller mortality from tuberculosis (mostly phthisis). The steel-melters had a 20 per cent. greater mortality than all males, but the other men working at high temperatures and the engine and crane-men had a smaller mortality. It is probable that all the records yield too low an estimate of the death-rate owing to the withdrawals of some of the less vigorous men.

Not less interesting than the high mortality from respiratory diseases is the low mortality from phthisis. Here is evidence, just as among coal-miners, of phthisis and respiratory diseases not moving together, while certain other occupations, such as printing, tailoring, and boot-making, provide instances of phthisis in excess, with respiratory diseases below normal. In other words, statistics do not favor the idea that phthisis develops from bronchitis and pneumonia.

Shop Standards of Fatigue. In a consideration of this subject, B. J. Newman² concludes that undue fatigue, wherever it occurs, must be regarded either as a symptom of disease, a sign of misdirection or waste of energy, or a reliable index to unhygienic working conditions of shop or factory reducing the efficiency of the worker.

If adverse mental processes are responsible for over-fatigue, the remedy is a question of placement, of fitting the worker to his job. If the tired feeling can not be charged to maladjustment, then diagnosis, treatment and other adaptation are in order. If the fatigue results from air poisoned from processes of manufacture, or vitiated from overcrowding, from monotony, or speeding up, then it must be said to involve society collectively and must be charged to industry as a social wrong.

Data are not complete for all industries, but sufficient study has been made to correct the more serious inroads on the welfare of the workman.

(2) *Mod. Medicine*, February, 1921.

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